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PROBLEMS OF SPACE BIOLOGY

Volume 8 - Adaptation to Hypoxia and Resistance of an Organism

V. N. Chernigovskiy, Editor

"Nauka" Press, Moscow, 1968

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION • WASHINGTON, D. C. • JULY 1969

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Selected Translations From:

PROBLEMS OF SPACE BIOLOGY

Volume 8 - Adaptation to Hypoxia and Resistance of an Organism

V. N. Chernigovskiy, Editor

Translation of "Problemy Kosmicheskoy Biologii. Tom VIII. Adaptatsiya k Gipoksii i Ustoychivost' Organizma"
Nauka Press, Moscow, 1968, pp. 5-146, 151-157, 166-181, 188-211, 230-243, 254-261.

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

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TABLE OF CONTENTS

Annotation..... vii

Acclimatization To Lowered Barometric Pressure As A Means Of Increasing Resistance To Various Extreme Factors.....1

The Effect Of Preliminary Acclimatization In Mountains On Man's Endurance Of Transverse G-Loads.....7

Physiological Reactions Of Man To The Effect Of Transverse G-Loads After Adaptation To High-Altitude Conditions.....17

The Effect Of Adaptation To Hypoxia Under Pressure-Chamber Conditions On Tolerance To Transverse G-Loads.....41

Characteristics Of Development Of The Adaptation Syndrone To Acute Hypoxia In Mountain Climbers.....50

The Effect Of Adaptation To High Altitude On Man's Tolerance Of Acute Hypoxia, High Temperature And Vestibular Irritations.60

CONCLUSIONS.....67

Effect Of Repeated Residence In Mountains On The Tolerance Of Mountain Climbers To Acute Hypoxia.....69

Tolerance Of Animals To Hyperoxia, Hypercapnia and High Temperature After Adaptation To Lowered Barometric Pressure...76

Effect Of Adaptation To Lowered Barometric Pressure On Tolerance Of Hypocapnia.....84

The Tolerance Of Animals To Acute Hypoxia After Conditioning To Physical Loads Under High-Altitude Conditions.....90

Mutual Effects Of Conditioning To Physical Loads And Adaptation To Hypoxic Hypoxia.....101

The Effect Of Prolonged Stay Under Conditions Of Lowered Barometric Pressure On Tolerance Of G-Loads.....105

The Effect Of Preliminary Interrupted Stay In A Rarefied Atmosphere On the Tolerance Of Rats To Transverse G-Loads....112

CONCLUSIONS....117

The Effect Of Adaptation To Conditions Of A Changed Gaseous Environment On Tolerance To G-Loads....119

METHOD....120

RESULTS....122

DISCUSSION....128

CONCLUSIONS....130

A Comparative Evaluation Of The Effectiveness Of Different Schedules Of Adaptation To Hypoxia....134

METHOD....135

RESULTS....137

CONCLUSIONS....140

The Effect Of Hypoxia On The Condition Of Defense Mechanisms Of The Organism Of A Mouse....142

METHOD....143

RESULTS....144

DISCUSSION....148

CONCLUSIONS....149

The Significance Of Certain Control Systems In Developing Adaptation To Hypoxia....152

The Role Of Certain Subcortical Formations In The Development Of Adaptation To Oxygen Deficiency....160

The Effect Of Aminazine On The Tolerance Of Animals To Acute Oxygen Starvation* (ABSTRACT ONLY)....164

The Role Of The Adrenal Glands In The Development Of Adaptation To Hypoxia....165

METHOD....166

RESULTS....167

Reaction Of The Blood To Hypoxia In Adrenalectomized And Hypophysectomized Rats* (ABSTRACT ONLY)....173

The Significance Of The Pituitary In The Development Of Adaptation To Hypoxia.....174
METHOD.....175
RESULTS.....176

Dynamica Of Change In The Osmotic Resistance Of Erythrocytes In Humans And In Animals During The Period Of Natural Acclimatization To High Altitude.....180
METHOD.....181
RESULTS.....181
CONCLUSIONS.....188
CONCLUSIONS.....189

Change In The Osmotic Resistance Of Erythrocytes In Adrenalectomized And Hypophysectomized Rats Placed Under High-Altitude Conditions* (ABSTRACT ONLY).....191

Repeated Exposure At "High Altitude" As A Method Of Revealing Latent Traces Of Adaptation To Hypoxia.....192

Duration Of The Reaction Of The Medulla Ossium To Acclimatization To Hypoxia.....204
METHOD.....205
RESULTS.....207
CONCLUSIONS.....209

The Mechanism Of Adapting White Mice To A Hypercapnic Gaseous Environment.....211
METHOD.....212
RESULTS.....212
CONCLUSIONS.....216

Enzymatic Activity Of Monoamino-Oxydase In Various Tissues And Organs Of Experimental Animals Acted On By Several Extreme Factors* (ABSTRACT ONLY).....218

Enzymatic Activity Of Monoamino-Oxydase In Various Tissues And Organs Of Experimental Animals Acted On By Several Extreme Factors* (ABSTRACT ONLY).....219

Activity Of Dehydrogenases Of Succinic And Lactic Acids Under Conditions Of Chronic Hypoxia* (ABSTRACT ONLY)..220

The Effect Of Hypoxia On The Reaction To Several Pharmacological Compounds.....221

CONCLUSIONS.....225

The Effect Of Antioxidants On Resistance Of The Organism And Certain Functions Under Hypoxia.....227

CONCLUSIONS.....233

The Problem Of The Mechanism Of The Effect Of Mexamine Under Hypoxia* (ABSTRACT ONLY).....235

The Effect Of Athletic Training And Acclimatization Under Middle-Altitude Conditions In The Caucasus On Several Characteristics Of The Peripheral Blood Of Young Field And Track Athletes.....236

METHOD.....237

RESULTS.....237

DISCUSSION.....240

CONCLUSIONS.....242

ANNOTATION

Data are cited in this book on adaptation of animal and human organisms to lowered barometric pressure, both under natural high-altitude conditions and under conditions in a pressure chamber. Also studied are the behavioral characteristics of persons who are first-time mountain climbers and those of experienced mountain climbers. The question concerning the role of physical exercise is discussed as it pertains to the development of adaptation to hypoxia.

It is established that adaptation to hypoxia of humans and animals increases resistance with respect to the effect of various adverse environmental factors: acute oxygen deficiency, increased gravity, high temperature of the environment, etc.

A special section of the book is devoted to studying the physiological mechanisms of adaptation to hypoxia and resistance of an organism. In this part the role of the different structures of the central nervous system and of certain endocrine glands is discussed.

This book is intended for the benefit of specialists working in the various fields of medicine and biology.

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ACCLIMATIZATION TO LOWERED BAROMETRIC PRESSURE AS A MEANS OF INCREASING RESISTANCE TO VARIOUS EXTREME FACTORS

(In Lieu of an Introduction)

The creation of methods which will permit expansion of the /5* boundaries of adaptation of the organism of animals and man to various adverse environmental factors and the scientific basis thereof is one of the most important problems encountered in modern biology and medicine. It is a problem that has attracted the attention not only of clinical physicians, biochemists, pharmacologists and physiologists concerned with work and athletics, but also of specialists working in the field of aviation and space medicine. These specialists are involved because of the possibility that in flights involving modern aircraft difficult stress situations may arise that would require the mobilization of all adaptation potentialities of the organism. In such case the success of the flight and, certainly safety in a number of instances, may be determined by the ability of the organism to adapt itself to various extreme factors: lowered barometric pressure, oxygen deficiency in the air inhaled, high G-loads, a significant elevation or lowering of the environmental temperature, etc. From the above, it becomes obvious that it is essential to establish scientific research to find means of raising the ability of an organism to adapt itself to different types of significant change in the environment.

Primarily there are two basic means of solving this problem that are possible: (a) using pharmacological compounds and various biologically active materials (vitamins, hormones, products of metabolism), which purposefully increase the adaptation potential of an organism, and (b) increasing the resistance of an organism by "acclimatization" of it to certain changes in the environment. This latter means is especially promisings since it promotes the /6 development of natural mechanisms of adaptation. However, the question does arise: for which of these factors involving change in the environment is it most feasible to promote adaptation? Experiments compiled in the field of athletic physiology, aviation and space medicine and mainly high-altitude physiology furnish a basis for assuming that training for oxygen deficiency is probably one of the most effective means of raising the adaptation potential of an organism. This opinion is based not only on the fact that oxygen starvation will lead to the development of non-specific functional stress, as several investigations have emphasized (Sel'ye, Lengli, Brüner and Klein) but also since oxygen deficiency

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* Numbers in the margin indicate pagination in the foreign text.

in itself is an essential element in the mechanism involved in many factors that are characteristic of flight and which act on an organism: increased gravity, high and low temperature, etc.

A great number of methods are known that will result in inducing a hypoxic state. Which of these should be selected for purposes of training? It is immediately apparent that there are two such methods which can be used to induce a "normal" physiological form of hypoxia. We are speaking here first of all about the intense muscular activity involved in various types of athletic exercise and secondly when an extended time is spent under conditions of a gaseous environment having a lowered partial oxygen pressure in the inhaled air which is the case at certain altitudes in mountains and is also encountered in high-altitude training in a pressure chamber and in the inhalation of gaseous mixtures which are poor in oxygen.

Training for the "physiological" form of hypoxia by raising the altitude in conjunction with muscular activity is apparently one of the most promising means of increasing the adaptation potential of an organism. Numerous physiologists have described the effectiveness of using this method for the most varied purposes (the training of pilots, athletes and for medical treatment of certain illnesses). Moreover, for almost 30 years now experiments have been periodically made on using adaptation to conditions of medium and high altitude both for the practical purposes of clinical medicine (Sirotinin et al) and for training of the healthy, including pilots (Sirotinin et al, Vladimirov et al, Hartmann et al). For this purpose several investigators have indicated the effectiveness of conducting systematic ascents in a pressure chamber (Strel'tsov, Vasilenko, Gazenko, Kuznetsov, Brüner and Klein).

At the present, several foreign specialists in the field of aviation and space medicine believe it to be feasible to include high-altitude training in the training schedule of astronauts. Apparently in this respect medical research abroad in recent years has been expanded, having been conducted in expeditions at various /7
altitudes, including research in specially organized high-altitude physiological laboratories. One such laboratory was even established in the Himalayas in the region of Mt. Everest at an altitude of 5800 m.

The basis of these developments is apparently the result of studies by Hurtado and Clark, Balk, and Velasquez et al. who showed that the Peruvian Indians who live at altitudes of 4000-4500 m, have exceptionally high physical endurance and resistance to acute hypoxia. Pressure-chamber studies, at altitudes of 9000 and 12,000 m, of reserve time (retention of the ability to function without oxygen) showed that in the Indians of Peru this time is significantly greater than in persons who are not adapted to high altitude. This furnishes a basis for assuming that the physiological picture of persons adapted to high altitude represents a

particular standard towards which we should tend in training.

Here it is only natural that the question should arise as to how high-altitude or pressure-chamber training should be carried out in order to produce results that are sufficiently effective. No scientific basis of a rational system of training for purposes of making a lengthy and maximally possible increase in the resistance of an organism to different extreme factors has been given to date. Study of this question, which is so important for practical application, is also one of the problems examined in the present research. However its successful solution will depend on studying the physiological mechanisms of an organism's adaptation to conditions of oxygen deficiency. Such an approach to the problem was solved by two basic means, based on which the investigations that were conducted in the period 1964 - 1966 were developed, both under conditions of high-altitude in the region of the Caucasus at altitudes of 2000 - 4200 - 5600 m, and in the laboratory in pressure chambers.

In experiments on animals several sides of the physiological mechanism of adaptation of an organism to lengthy stay under conditions of a rarefied atmosphere were primarily studied; in similar studies with humans, the effectiveness of the selected program of "acclimatization" was basically calculated.

Thus, investigations with humans had a practical purpose; here it was shown that people who have never lived in the mountains and who remain for a period of a month in mountains at altitudes from 2000 to 4200 m with sporadic ascents to altitudes of 5000 - 5600 m will have a pronounced increase in their resistance to acute hypoxia and to the influence of transversely directed accelerations. These data, which have been found at the present time only on a relatively small number of individuals, suggest the expectation that "acclimatization" under high-altitude conditions can be successfully used in a system of preparation and training of athletes, astronauts and members of other specialities which periodically require of man the ability to undergo extreme degrees of physical and intellectual/8 stress.

In making such investigations it would seem that we can never be satisfied only by determining the resistance of the examinee to various influences prior to and after high-altitude training, but it is essential that the dynamics of development of the adaptation syndrone be studied so as to find a fixed correlation between the proper adaptation improvements and the effects attained as a result of training.

The results of the study conducted with mountain climbers also confirm the feasibility of using high-altitude training. The high resistance to acute oxygen starvation and to the effect of G-loads, found in the majority of mountain climbers even before their next trip into the mountains, permits assuming that with a rationally

constructed program of "high-altitude" training, and probably pressure-chamber training as well, we can assume the attainment of a lengthy, at least for several months, retention of the increased resistance achieved in the process of training to adverse environmental conditions. The negative results obtained in studying the effect of high-altitude adaptation for the resistance of an organism to the influence of elevated environmental temperature will require further testing since there does exist a basis for assuming that under the temperature conditions of high-altitude adaptation, they can be avoided. It is essential, from the viewpoint of practical utilization of high-altitude training, that we consider the fact that the most distinct positive effect was found in persons who had relatively low resistance to the effect of extreme factors prior to the mountain-climbing expeditions. At the same time, persons remaining under high-altitude conditions and who possess a previously high resistance to the effect of G-loads and acute hypoxia, increased their resistance to the above factors relatively little. From the above discussions we can conclude that in preparing a flight crew, astronauts and probably athletes it makes sense to use high-altitude training mainly for those individuals whose previous resistance to the effect of extreme factors is low.

Analysis of the data revealed that a significant increase in respiration during acute hypoxia is characteristic of the majority of mountain climbers, with respect to which even at the present time considerable attention should be paid, in the process of adaptation to hypoxia, to respiration by trying to increase the effectiveness of this function to its maximum. This position corresponds fully to the results of investigations by Lauer, Kolchinskaya, Seredenko and others who found an increasing optimization of the exhalation function in persons who have shown a significant increase in their resistance to the effect of acute hypoxia and transversely directed accelerations after undergoing high-altitude training.

In conclusion, let us look briefly at the results of experiments directed toward studying the physiological mechanism of adaption to hypoxic hypoxia of animals. /9 The process of acclimatization to a lengthy period of time under conditions of a gaseous environment with lowered partial pressure of oxygen will apparently lead to an essential rebuilding of many of the control systems of an organism. There exist in the literature several discussions which differ from one another to a greater or lesser degree, that reflect the participation of functional systems of the organism in adaptation (Strel'tsov, Barcroft, Charniy, Gellhorn et al, Barbashova). Considerable significance is given by several authors in such case to changes in the functional state of the central nervous system and to the endocrine glands. Thus, an essential role is played by the adrenal and pituitary glands at various stages of adaptation, as noted by Sel'ye and Lengli. The question as to the significance of the nervous system in the development of adaptation to hypoxia has as yet been studied very little. Basically at the

present time only the significant role of the sympathetic nervous system has been mentioned (Barbashova). The significance of the cortex of the major hemispheres and the structure of the gray matter in the development of adaptation has as yet been studied only slightly.

We assume that adaptation to hypoxia, just as to many other influences, can be studied as a problem of memory. Such resistration (remembering a new situation) is carried out at various levels, in many cellular structures of an organism and obviously first of all in the control system. This latter is of interest to the authors of this collection in explaining the role of the endocrine glands and the nervous system in the development of adaptation.

In the papers published in this collection, experimental data are given which characterize the development of adaptation to lowered barometric pressure in animals who have had their most important control systems such as the adrenal glands, the pituitary glands, the cortex of the major hemispheres and the cerebellum operationally disconnected. The results of the investigations showed that after removing these systems it is possible to produce an adaptation development which has certain characteristics. Substantial data relative to the effectiveness of the various systems of acclimatization and the significance of the physical load in the process of adaptation to hypoxia were also obtained in experiments on animals.

Many investigators (Sirotinin, Armstrong et al) believe that the effectiveness of systematic pressure-chamber training is low and can not compare with residence under high-altitude conditions. The results of experiments on animals show that gradual adaptation is most effective in a pressure chamber when altitudes up to 7000 m are attained.

Thus, there exist sufficient theoretical premises for use in training in a pressure chamber, with respect to which at the present time it is opportune to pose the question of design and manufacture /10 of special large scale "acclimatization" pressure chambers in which it is possible for several persons to remain for a long period of time involving the wide utilization of different types of physical loads rather than under conditions of relative hypodynamia as in previous research.

The authors hope that the materials in this collection will be of aid to physicians, physiologists and biologists who are studying the problem of adaptation of animal and human organisms to hypoxia.

The authors wish to extend their appreciation to Professor N.N. Sirotinin of the Academy of Medical Sciences, USSR, to Doctors of Medical Sciences N.V. Lauer and A.Z. Kolchinskaya for their kind

assistance and for the opportunity of conducting the research in the laboratory of the Academy of Sciences of the Ukrainian SSR under high-altitude conditions as well as for their valuable advice in analyzing the data presented here.

THE EFFECT OF PRELIMINARY ACCLIMATIZATION IN MOUNTAINS ON MAN'S ENDURANCE OF TRANSVERSE G-LOADS.

A.R. Kotovskaya, P.V. Vasil'yev, R.A. Vartbaronov and S.F. Simpura.

ABSTRACT: In investigations on humans, the effect was studied of a 1-5 month residence under high-altitude conditions on their resistance to the effect of transversely directed G-loads (+Gx). The experiments were conducted on mountain climbers and on persons who had not been adapted to hypoxia. It was established that residence under high-altitude conditions produced an expansion of the functional potentialities of the organism and guaranteed a significant increase in its resistance to the effect of G-loads. The increase in resistance to G-loads was +1.7 on the average. The authors consider it feasible to use this method for increasing the resistance of an organism for the practical purposes of pre-flight training of astronauts.

To increase man's resistance to the effect of transversely directed G-loads, it is of fundamental significance to develop methods which will permit increasing the compensatory possibilities of the organism. Here it is feasible to use a nonspecific adaptation which will permit increasing the resistance of the organism to a number of adverse environmental factors. /11

Research has been reported in the literature which indicates the effectiveness of using in this plan nonspecific conditioning. The greatest number of such investigations have involved the problems of adaptation to hypoxic hypoxia, the study of which is of exceptionally great importance for practical problems of aviation and space medicine. In the experiments of Z.I. Barbashova et al, G.A. Vasil'yev, I.V. Korostovtseva, N.N. Sirotinin [3,4,13,18] and many others it has been shown that animals adapted to lowered partial oxygen pressure revealed a high tolerance to the effect of chemical agents (strychnine, cyanide, caffeine), heat or cold, to radiation and to the effect of other factors. On the other hand there do exist data which indicate a favorable effect of physical conditioning on tolerance of hypoxia, cooling, and the effect of poisons and radiation [2,11,12,15]. In these investigations the effectiveness of nonspecific adaptation to a significant degree depended on the schedule selected for conditioning to physical load and hypoxic hypoxia. In particular, V.Ya. Rusin [17] showed that

the complex use of muscular conditioning and pharmocological means was found to be more effective than using each of these means alone. /12

In the research by Ye.V. Loginova (see this collection, p. 93 of original text, p. 101 of the translation) it was found that under conditions of hypoxia several forms of muscular load facilitate acquisition of a high adaptation effect. All this would permit us to assume that the preliminary prolonged effect of moderate hypoxia and muscular conditioning may have a favorable effect when a subsequent gravitational stress occurs. And in fact in the work of Dudarev, Vasil'yev, Belaya there was shown an increase in the tolerance to G-loads in animals that had been adapted to hypoxia [5,10].

P.V. Vasil'yev and N.N. Uglova [8,9], in experiments on animals, established that the survival of acclimatized white mice, rats and guinea pigs under the influence of large G-loads (up to 40 units) was 1.5 - 2 times higher than in the control animals. This effect was retained for a period of the first 2 - 3 weeks following completion of the adaptation.

Active adaptation of animals to conditions of high altitude by systematic physical conditioning of a static nature was found to be more effective than passive residence at high altitude. With active adaptation the survival of the animals under the influence of G-loads was 25% higher than with passive adaptation.

Klein, Bruner and Jovy studied nonspecific stress reactions in 3 subjects to the effect of different factors of the environment before and after a 4-week residence at an altitude of 6300 m in the Andes [19]. The criterion of the expression of stress was the improvements in the eosinophils and the corticosteroids of the blood.

According to the authors' data the improvenemts in these blood characteristics after the effect of G-loads in the direction of the head - pelvis for a period of 10 minutes was 2.5 units less than after background tests prior to excursions into the mountains. Residence at an altitude of 6300 m under conditions of changing climate and the carrying out of increased physical activity, in the authors' opinion, results in a rather noticeable adaptation in the pituitary-adrenal system and distinctly improves the reactions of blood circulation, respiration and other physiological systems under the influence on man of stress loads encountered in flight (hypoxia, G-loads, etc.).

The possibility of increasing man's tolerance to the effect of transversely directed G-loads after residence under high-altitude conditions was established by us in 1964 after completing the first expedition [6,7,14,16].

Taking into account the increase in the effect of nonspecific adaptation involving the complex use of the method of hypoxia and

muscular conditioning, we considered it to be feasible to determine the possibility of raising the organism's tolerance of the effect of G-loads following preliminary residence under high-altitude conditions.

The basic problems of the investigation were: /13

Study of the background tolerance to the effect of G-loads in mountain climbers and subjects not adapted to high altitude;

Study of the tolerance of G-loads after residence under high-altitude conditions;

Determination of the duration of retention of the positive effect of adaptation.

The investigations were carried out on 28 subjects, from which 8 were mountain climbers who had participated in sports for more than 10 years, 8 were persons who were unadapted to hypoxia and 12 were person (the control group) who did not participate in the high-altitude expedition. Acclimatization to hypoxia was carried out in the mountainous regions of the Caucasus (1964-1965) and Tyan'-Shan' (1964). The group of eight was first placed in the mountainous regions of the Caucasus at an altitude of 2000 m for a period of two weeks and at 3800 - 4200 for the next two weeks. Along with residence at the base camp, the subjects made periodic ascents to an altitude of 5600 m (Mt. Elbrus). The group of mountain climbers (6 subjects) resided also in the base camp in the town of Terskol at an altitude of 2000 m and made three ascents of increasing difficulty to altitudes of 3500 - 4500 m. Two of the mountain climbers were subjected to acclimatization in the mountainous region of Tyan'-Shan' for a period of 1.5 months in the base camp at an altitude of 4000 m with periodic ascents to an altitude of 7000 m.

The times of adaptation and the distribution of subjects are showen in Table 1.

TABLE 1. DISTRIBUTION OF SUBJECTS AS A FUNCTION OF TRAINING CONDITIONS.

Group	Total	Conditioned to G-load tolerance		Region of acclimatization in mountains	Duration Of acclimatization, days
		before acclimatization	after acclimatization		
Mountain climbers	8	6	6	Caucasus	35
		2	2	Tyan'-Shan'	41
Preadapted subjects	8	8	8	Caucasus	33-35
Control (Moscow)	12	12	-		-

In carrying out the investigations on a centrifuge the maximum size of the peak G-load was determined at which the first signs of functional disorders appeared from the side of the physiological systems of the organism. The angle of lift of the back of the chair from the "horizontal" was 25° and only in one case was it 10° (the /14
subject P-s). The gradient of increase in the G-load was equal to 0.2 units/sec. The basic criterion for evaluating the adaptation to G-loads was the change in the maximally tolerable value of the peak G-load. The most often encountered signs of maximal tolerance of G-loads were the visual disorders in the form of "gray" or "black" veils. We also took into account the data from recordings of the basic physiological functions, the time of their recovery during the period of after-effects, data from oral and written response of the subject and the results of doctor's examination after rotation in a centrifuge. The original tolerance of transverse G-loads was determined no less than in two tests, and also after 3 - 15 days and after 1 - 2, and in several instances 3 months following completion of the high-altitude expedition.

In the course of the experiment a constant visual observation was carried out on the subject using television, and two-station radio communication was regularly maintained.

Determination of the tolerance before going into the mountains showed that the mountain climbers, in spite of the large gap following their previous residence in the mountains (10 - 11 months), were found to be more tolerant of transverse loads than those who had not resided in the mountains. Thus the limit of tolerance of G-loads for the eight mountain climbers was on the average 10.5 units and exceeded with reliability (more than 0.95) the average value (9.4 units) that was established in the 19 subjects of the control group (Table 2).

TABLE 2. AVERAGE TOLERANCE OF G-LOADS IN THE ORIGINAL STATE FOR MOUNTAIN CLIMBERS AND SUBJECTS OF THE CONTROL GROUP.

Group	Number of subjects	G-Load tolerance, units
Mountain climbers	8	10.5±1.2
Control	19	9.4±0.9
Reliability of differences between groups		>0.95

TABLE 3. CHANGE IN THE MAXIMALLY TOLERABLE SIZE OF THE G-LOAD FOLLOWING RESIDENCE UNDER HIGH-ALTITUDE CONDITIONS.

No.	Subject	Tolerable G-load, units		Difference in tolerance
		In original state	After high altitude	
		Mountain Climbers		
1.	K-v	11.0	12.0	+1.0
2.	S-t	10.5	11.8	+1.3
3.	G-r	8.0	10.8	+2.8
4.	B-n	10.4	12.3	+1.9
5.	N-v	9.2	11.0	+1.8
6.	Bul-v*	12.5	14.1	+1.6
7.	B-v*	10.8	12.2	+1.4
	Average	10.3±1.4	12.0±1.1	+1.7±0.6

No.	Subject	Tolerable G-load, units		Difference in tolerance
		In original state	After high altitude	
		Unconditioned Subjects		
1.	Sh-k	8.8	10.0	+1.2
2.	V-ko	9.8	11.2	+1.4
3.	Ku-s	9.6	9.0	-0.6
4.	P-s**	9.5	11.0	+1.5
5.	A-v**	11.8	11.5	-0.3
6.	M-v	9.6	12.2	+2.6
7.	G-va	10.0	12.1	+2.1
8.	K-as	9.2	13.0	+3.8
	Average	9.5±0.4	11.25±1.5	+1.75±1.4

[Notes for Table 3 on next page]

* Mountain climbers who participated in the expedition to Tyan'-Shan'.
** Subjects P-s and A-v were not included in the statistical processing since, in the first case unlike all the others, the angle of lift of the back of the chair was 10°, and in the other case under high-altitude conditions no adaptation was noted (signs of altitude sickness).

Consequently, the tolerance to the effect of transversely directed G-loads in the mountain climbers in the original state was higher than in subjects of the control group on an average by 1.1 units.

After residence in the high-altitude camp for a period of 35 - 41 days the tolerance to G-loads in all of the mountain climbers increased on the average by 1.7 ± 0.6 units. The maximal increase in tolerance was noted in the mountain climber G-r (by 2.8 units) in whom the original tolerance was the lowest (8 units). Individual improvements in tolerance to G-loads of the subjects after 3 - 15 days following descent form the mountains to the plains are shown in Table 3. /15

Unlike the mountain climbers who showed an identical directionality in the changes of tolerance following residence at high altitudes, in the subjects of the control group no increase was noted in tolerance of G-loads in several instances. Out of the eight unconditioned subjects, the tolerance to G-loads increased in six +1.2 to +3.8 units. In subject A-v (No. 5) in whom, during the time of residence at high altitudes, clear indications of altitude sickness were noted, the tolerance to transverse G-loads did not change substantially, and in subject Ku-s (No. 3) the tolerance to G-loads was found to be somewhat lowered.

With the action of G-loads following previous residence in the mountains in the overwhelming majority of cases an increase was noted in the threshold of appearance of visual disorders (Fig. 1).

The state of increased resistance to G-loads in the mountain climbers was retained for more than one, two or even three months with a pronounced tendency to recovery of the original level (Fig. 2).

The condition of increased tolerance in 6 subjects who resided in mountains for the first time was retained for a period of 2 - 3 months just as in the mountain climbers. However the dynamics of the changes in tolerance had greater individual differences (Fig. 2).

Increase in the nonspecific resistance to G-loads following residence under high-altitude conditions is confirmed also by the data from subjective response of the subjects. After adaptation

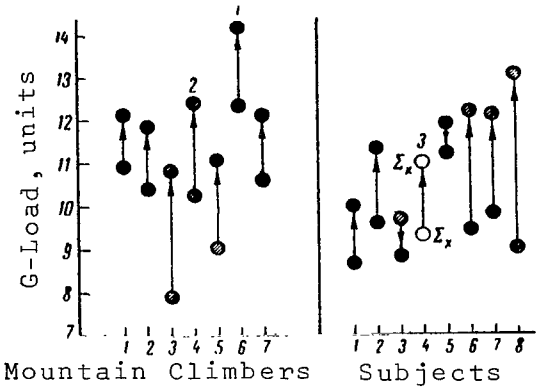

Fig. 1. Change in the Threshold of Appearance of Visual Disorders in Subjects Acted on by G-Loads Following Residence Under High-Altitudes Conditions (on the 13 - 15 Day). 1. Black Veil; 2. Gray Veil; 3. No Visual Disorders; Σ_x is the Extrasystole. Subjects P-s (No. 4) and A-v (No. 5) were Subjected to the Effect of G-Loads a Month after Adaptation. /16

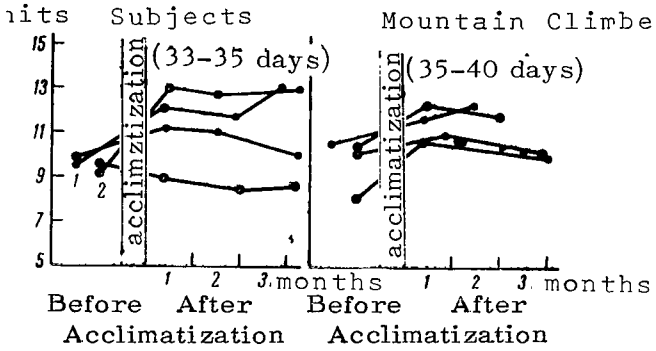

Fig. 2. Change in the Level of Tolerance to G-Loads in 4 Subjects and 4 Mountain Climbers for a Period of 1.5 - 3 Months after Acclimatization in Mountains. The Designations are the same as in Figure 1.

in the mountains in 50% of the cases (4 mountain climbers and 4 other participants in the expedition) there was noted subjectively a better tolerance to the G-loads. This was expressed in the decrease in the perception of pressure in the chest, improvement in the overall state of being, lack of sensations of sickness, less difficulty in breathing, etc., in spite of the large values attained after adaptation to G-loads. In the other cases (7 subjects) the subjects did not note any pronounced difference in the subjective sensations. In the overwhelming majority of cases, the subjects, following residence in the mountains, subjectively noted a pronounced improvement, manifested in the delayed appearance of visual disorders. /17

Improving the tolerance to transversely directed G-loads after residence under high-altitude conditions has also been noted by other authors [1].

Thus, the materials which we have cited permit us to confirm that a relatively short-term residence under high-altitude conditions is sufficiently effective for increasing the tolerance of man to the effect of transversely directed G-loads. In large part the tolerance to G-loads was increased after 32 - 41 days residence in mountains on the average in all mountain climbers by 1.7 units and

in subjects with first-time residence at high altitudes by 1.75 units.

Let us look at the duration of retention of the positive effect; almost in all cases with repeated tests in a centrifuge for a period of 1 - 3 months the maximal tolerance of G-loads still exceeded the original level (Fig. 2). Repeated stays in the mountains for a period of 10 years and more by the mountain climbers resulted in the adaptation effect being observed in them not only for a period of 2 months following successive ascents, but after 10 - 11 months. However, taking into account the data from the change in resistance in mountain climbers and those subjects living under high-altitude conditions for the first time, we may assume that individual characteristics and systematic conditioning play a large role in the process of nonspecific adaptation.

Two cases are worthy of attention when, following residence under high-altitude conditions, no increase in tolerance to G-loads occured. In one of the subjects (A-v) this obviously was caused by the onset of altitude sickness; in the other (K-s) the decrease in tolerance to G-loads has no satisfactory explanation.

Thus, the investigations carried out showed that residence under high-altitude conditions facilitated widening the functional possibilities of the organism and guaranteed a pronounced increase in its resistance to the effect of transversely directed G-loads. Increase in the adaptation possibilities occured as a result of /18
the combined effect of two basic factors - intense muscular activity and prolonged residence under environmental conditions with a lowered partial oxygen pressure.

The obtained results permit examining the method used for acclimatization in mountains as one of the effective methods of nonspecific conditioning. The time of retention of the positive effect of adaptation indicates the feasibility of using this method for increasing the resistance of the organism for preflight training of astronauts.

Further investigations in this direction must provide for an in-depth study of the possible mechanisms of nonspecific adaptation and also make the optimal relationship and the specific value of the physical factors associated with the term "acclimatization in mountains" more specific.

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PHYSIOLOGICAL REACTIONS OF MAN TO THE EFFECT OF TRANSVERSE G-LOADS AFTER ADAPTATION TO HIGH-ALTITUDE CONDITIONS.

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ABSTRACT: In investigations on humans the effect was studied of a 1-5 month residence under high-altitude conditions on the physiological reactions of man acted on by transverse G-loads ($+G_x$); the experiments were conducted on mountain climbers and on persons who had not been adapted to hypoxia. EKG's and EEG's were measured as were blood pressure, respiration rate, respiration and gas exchange as well as the time of motor reaction to light signals. The authors showed that residence under high-altitude conditions produced an expansion of the functional potentialities of the organism, thus guaranteeing a significant increase in its resistance to the effect of G-loads. The positive effects of acclimatization to hypoxia were revealed in a number of readings from the cardiovascular and respirational systems. Possible mechanisms of of the improvements attained are discussed in the article.

At the present time, thanks to the large number of investigations, it has been established that under the effect of prolonged transverse G-loads, one of the basic pathogenetic mechanisms is the development of circulatory and hypoxic hypoxia. A prolonged effect from G-loads produces a disruption in the oxygenation of the blood, caused by changes in the mechanics of breathing and resistribution of the blood in the lungs. A decrease in the oxygen in the arterial blood and the overall changes in the hemodynamics may lead to a disruption of the oxygen balance in the organism. Tests by athletic physiologists and those of aviation medicine and high-altitude physiologists indicate that one of the effective means of increasing the adaptation reserve of the organism is adaptation to conditions of hypoxia. Here the combination of intense muscular activity and prolonged residence under conditions of a gaseous environment with a lowered partial oxygen pressure is one of the promising means of increasing the adaptation possibilities of the organism to the effect of a number of extreme factors including G-loads.

The large amount of research has shown that animals adapted under conditions of hypoxia possess an elevated resistance to acute oxygen starvation, the penetration of radiation, the toxic effect of poisons, etc. At the present time there is no unified opinion

concerning the mechanism of raising this nonspecific resistance. The majority of investigators assume that the stimulation of organs and systems participating in the transport of oxygen is of great significance, and several authors indicate also tissue mechanisms of adaptation [2,3,4].

We are interested in the question concerning the possibility and feasibility of using adaptation to high altitude as a means for increasing the resistance of man to the effect of transversely directed G-loads. Therefore the purpose of these investigations was to explain the possibilities of raising the tolerance of the organism to the effect of G-loads after preliminary residence under high-altitude conditions and also to study several sides of the physiological mechanisms that determine the change in tolerance. /20

The adaptation to hypoxia was carried out in the mountainous regions of the Caucasus and Tyan'-Shan'.

The conditions of acclimatization, the control of subjects as well as the method of determining the maximal tolerance have been described in a previous article in this collection. To evaluate the characteristics of the processes of nonspecific adaptation during rotation in a centrifuge we recorded the following signs of physiological reactions: pulse rate, EKG (in Nebu leads), EEG (in 2 bipolar "forehead - crown" and 2 unipolar "forehead - left parietal" leads), arterial pressure in the vessels of the concha auriculae and arm, the respiration rate, pulmonary ventilation and gaseous metabolism; we determined the visual acuity and the latent period of the motive response reaction to light signals.

As we establish earlier, residence in mountains for a period of 1 - 1.5 months increased the tolerance to G-loads in six out of the eight subjects, unadapted to high altitude, by 2.2 ± 1.0 units; in all of the mountain climbers by 1.7 ± 0.6 units.

To evaluate the mechanisms of adaptation of the organism to the effect of G-loads it was important to trace the changes in certain physiological reactions in man prior to and following residence under conditions of the high-altitude expedition. Therefore in studying the obtained data we took into account the dynamics and the direction of the physiological reactions during the time of G-loads effect, and also the time of their recovery in the after-effect period. Furthermore, it seemed important to find the difference in tolerance to G-loads in mountain climbers who had been repeatedly adapted to conditions of high altitude and in those subjects who were exposed to these conditions for the first time.

Analysis of the data showed that the direction of the physiological reactions during the time of the G-load effect in the mountain climbers and in the subjects was the same. In the original state, in proportion to the nearness of the rotation, in practically all the mountain climbers and subjects signs were noted of emotional

stress before the test which were manifested in the increase in pulse rate and elevation in arterial pressure. After residence under high-altitude conditions these changes prior to rotation differed slightly from the background changes (Table 1). However, the pulse rate after descent from high altitude before the test was somewhat higher than before the background rotations (the differences are reliable).

Study of the dynamics of change in the frequency of heart contractions during the time or rotation with identical values of the G-load (8 - 9 units) showed that in the majority of cases after adaptation under high-altitude conditions the pulse rate was at a higher level than with the background test. On the average the pulse rate exceeded the level registered in the original determination, in the mountain climbers by 12 and in the subjects by 10 beats/min.

TABLE 1. CHANGE IN PULSE RATE AND ARTERIAL PRESSURE IN MOUNTAIN CLIMBERS AND SUBJECTS BEFORE THE EFFECT OF G-LOADS PRIOR TO AND FOLLOWING RESIDENCE UNDER HIGH-ALTITUDE CONDITIONS (MEAN VALUES). /21

Group	Characteristic	Before High Altitude		After	
		for 5 min.	for 1 min.	for 1 min.	for 1 min.
Mountain Climbers	Systolic pressure, mm Hg	119±5.0	127±5.0	113±13.0	123±14
	Pulse Rate, beats/min	68±4.5	82±12.3	75±3.0*	84±10.2
Unconditioned Subjects	Systolic pressure, mm Hg	117±8.0	122±10.0	115±6.0	121±8.0
	Pulse Rate, beats/min	66±4.0	78±10.8	70±11.0	80±8.4

* The reliability of differences in the characteristics found after adaptation at high altitude is >0.95; in the other cases the differences are not reliable.

Comments: 1. The reliability of differences was determined by two methods: by comparison of the data which is uniform in time before and after residence at high altitudes and also data obtained after 5 and 1 minute before rotation on a centrifuge. 2. The changes in these characteristics for 1 minute before rotation in comparison with the data from the 5-minute readiness are statistically reliable (P>0.95).

However, in this case there appeared individual differences (Table 2). As follows from this table, in three of the subjects

(Bul-ov, A-v and P-s) after residence at high altitudes the pulse rate with a given value of the G-load was 8 - 10 beats/min lower than in the original rotation; in one of the subjects (V-ko) there was no difference and in ten of the others it was higher than the background level by +9-+34 beats/min.

It was of interest to analyze the frequency of the heart contractions under the influence of G-loads before and after residence at high altitudes as a function of the original level before rotation. We found that in 12 cases out of 15 the pulse rate after high altitude for 5 minutes before the test on a centrifuge was slightly higher than prior to expeditions into the mountains. In this respect the relative increase in pulse rate (with respect to the original value, taken for 100%), at the level of the G-load of 8 - 9 units after high altitude was individually different. Here the mean values reliably exceeded the original data (Table 3).

The recovery time of the frequency of heart contractions and arterial pressure after G-load effect was found to be different in the various subjects. In the majority of cases in spite of the fact that the value of the attained G-load after residence at high altitudes almost always exceeded the original, this period was either shortened or was the same as the background value (Table 4).

The total recovery time of the characteristics of the cardiovascular system decreased insignificantly only in four cases out of the 15; the difference in the length of normalization time in 4 of the subjects was from 1 to 4 min.

No correlation between the recovery time of the characteristics of the cardiovascular system and differences in the G-load tolerance was noted. Thus, for example, in one of the subjects (K-as) with the least increase in G-load tolerance by +3.8 units the recovery time of these characteristics did not differ from the original, and in another (B-v) on the contrary with a small increase in tolerance by 1.4 units it was found to be somewhat more extended than following the background test.

Analysis of the electrocardiograms showed that in the majority of cases under the effect of G-loads prior to the high-altitude expedition the phenomena of sinusal pachycardia were noted with characteristic changes from the side of the intervals and the amplitude of the waves, sharper characteristics in disruption of the rhythm in the form of single extrasystoles [5, 13, 16].

No pronounced difference in the changes in the electrocardiographic characteristics under the influence of the G-load in the mountain climbers and the subjects was noted. However, the value of the G-load attained in the mountain climbers as a rule was greater than in subjects who were exposed to mountainous conditions for the first time.

TABLE 2. FREQUENCY OF HEART CONTRACTIONS (BEATS/MIN) IN SUBJECTS ACTED ON BY 8-9 UNIT G-LOADS BEFORE AND AFTER RESIDENCE UNDER HIGH-ALTITUDE CONDITIONS.

Group	Name	Before adaptation	After adaptation				Changes in G-Load tolerance, units	
			After 10-15 days	Difference	After 2.5-3 months	Difference	After 10-15 days	After 2.5-3 months
Mountain climbers....	K-v	114	125	+11	132	+18	+1.0	+1.3
	S-t	135	144	+9	—	—	+1.3	—
	G-r	126	150	+24	150	+24	+2.8	+2.2
	B-n	153	162	+9	168	+15	+1.9	+1.4
	B-v	110	144	+34	—	—	+1.6	—
	Bul-ov	140	132	-8	—	—	+1.4	—
	N-v	146	—	—	150	+4	—	+0.8
Average.....		130±16	143±13	+13±14	150±15	15±8*	+1.7±0.6**	+1.4±0.6
Unconditioned subjects....	Sh-k	101	110	+9	—	—	+1.2	—
	V-ko	120	120	0	120	0	+1.4	+0.2
	Ku-s	143	165	+22	145	+2	-0.6	-0.9
	M-v	114	136	+22	120	+6	+2.6	+3.4
	G-va	114	130	+16	—	—	+2.1	—
	K-as	108	130	+12	120	+12	+3.8	+3.8
	A-v	130	120	-10	120	-10	-0.3	+0.3
Average.....		119±12	129±18	+10±12	125±11	+2±8	+1.5*±1.5	+1.4±2.1
Selected average.....		117±14	130±19	+12.5±9*	126±13	+5±5	+1.75*±1.4	+1.6±2.3

*P>0.95.
**P>0.99.

Comments: 1. The selected average was computed for all unconditioned subjects other than A-v in whom there was no adaptation to altitude. 2. The criteria of significance were determined only for the changes in the cited characteristics.

TABLE 3. PULSE RATE DURING THE TIME OF G-LOAD ACTION WITH A VALUE OF 8—9 UNITS BEFORE AND AFTER ADAPTATION UNDER HIGH-ALTITUDE CONDITIONS AFTER 10 - 15 DAYS.

Group	Name	Changes in G-load tolerance, units	Before adaptation			After adaptation			Difference	
			for 5 min. before rotation	during the time of effect	increase, %	for 5 min. before rotation	during the time of effect	increase %	for 5 min. before rotation	increase %
Mountain climbers	K-v	+1.0	65	114	+75	74	125	+69	+9	-6
	S-t	+1.3	72	135	+87	78	144	+85	+6	-2
	G-r	+2.8	66	126	+90	72	150	+108	+6	+18
	B-n	+1.9	75	153	+104	78	162	+107	+3	+3
	B-v	+1.6	62	110	+77	72	144	+100	+10	+23
	Bul-v	+1.4	72	140	+94	78	132	+69	+6	-25
Average		+1.7±0.6	+69±5	130±16	+88±11	78±3	143±13	+90±18	+6.7±2.5	+2±17
Unconditioned subjects	M-v	+2.6	66	114	+73	80	136	+70	+14	-3
	G-va	+2.1	66	114	+73	72	130	+80	+6	+7
	K-as	+3.8	66	108	+63	66	120	+81	0	+18
	A-v	-0.3	72	130	+80	72	120	+66	0	-14
	V-ko	+1.4	63	120	+90	66	120	+81	+3	-9
	Ku-s	-0.6	66	143	+116	66	165	+150	0	+34
	Sh-k	+1.2	60	101	+68	66	110	+66	+6	-2
Average		+1.5±1.6	66±4	119±14	+80±18	70±11	129±17	+85±29	+4±5	+4±17
Selected average		1.75±1.4	65±2.5	117±14	+80±20	69±6	130±19	+88±31	+5±4	+7.5±15

Comment: Mountain climber N-v who was tested after 2.5 months following residence at high altitude, was excluded from the table. The other designations are the same as in Table 2.

TABLE 4. RECOVERY TIME OF PULSE RATE AND ARTERIAL PRESSURE DURING THE PERIOD OF AFTER-EFFECT OF G-LOADS PRIOR TO AND FOLLOWING RESIDENCE UNDER HIGH-ALTITUDE CONDITIONS. /24

Group	Name	Difference in G-load tolerance, units	Total recovery time, min.		
			Before	After	Difference
Mountain climbers	K-v	+1,0	5	5	0
	S-t	+1,3	8	7	−1
	G-r	+2,8	4	4	0
	B-n	+1,9	6	3	−3
	Bul-v	+1,6	2	6	+4
	B-b	+1,4	4	6	+2
Unconditioned subjects		$M \pm \sigma$			+0,3±2,4
	Sh-k	+1,2	6	2	−4
	V-ko	+1,4	3	2	−1
	K-s	−0,6	5	5	0
	P-s	+1,5	4	7	+3
	A-v	−0,3	6	5	−1
	M-v	+2,6	1	2	+1
	G-va	+2,1	5	5	0
	K-as	+3,8	6	6	0
		$M \pm \sigma$			−0,3±2,0

Comment: Measurement error in the recovery time did not exceed ± 1 min.

Following residence under high-altitude conditions, changes in the electrocardiographic characteristics were approximately the same as during the background investigation. However, in this case there appeared individual characteristics which deserve special study. /25

Thus, in the subject P-s with repeated background rotations on a centrifuge there were recorded on the EKG signs of disruption in the heart rhythm in the form of a ventricular extrasystole of bigeminy type, which also served each time as the reason for cessation of the test (Fig. 1). Analogous changes in the EKG were recorded with the development of acute hypoxia in the pressure chamber and also with a physical load (20 quarts for 40 sec).

These disruptions in the heart rhythm with a cessation of the load test disappeared and were not noted under conditions of rest which caused us to evaluate them as an extrasystole of "stress".

After a month's residence under high-altitude conditions, this subject was again subjected to tests of two types: with determination of the maximally tolerable G-load value and also with a G-load of 10 units which was constant in value for a period of 20 sec ("rest time"). It was found that following hihg altitude under the effects of G-loads in the form of "rest time" on the EKG there was not registered any extrasystole. At the time of the test following 1.5

months after residence in the mountains for determining the maximally tolerable value of the G-load on the EKG we noted the same disruptions in rhythm of the cardiac activity as with the background test. However, these deviations on the EKG appeared with a G-load of 11 units whereas with the background rotation they always appeared with a G-load of 9.5 units (Fig. 2). Furthermore, the time of normalization of the pulse rate in this subject in spite of the large value of the G-load attained, decreased by 1 minute in comparison with the control group. Such a positive result was noted during the test in the pressure chamber and under physical load.

Furthermore, in the mountain climber B-na and in all of the control subjects on the EKG there were registered individual ventricular extrasystoles. After residence in the mountains under the action of a larger G-load (by 1.9 units) than with the background test, no sign of disruption in the heart rhythm was noted. Although the causes which lead to the onset of extrasystoles during /26

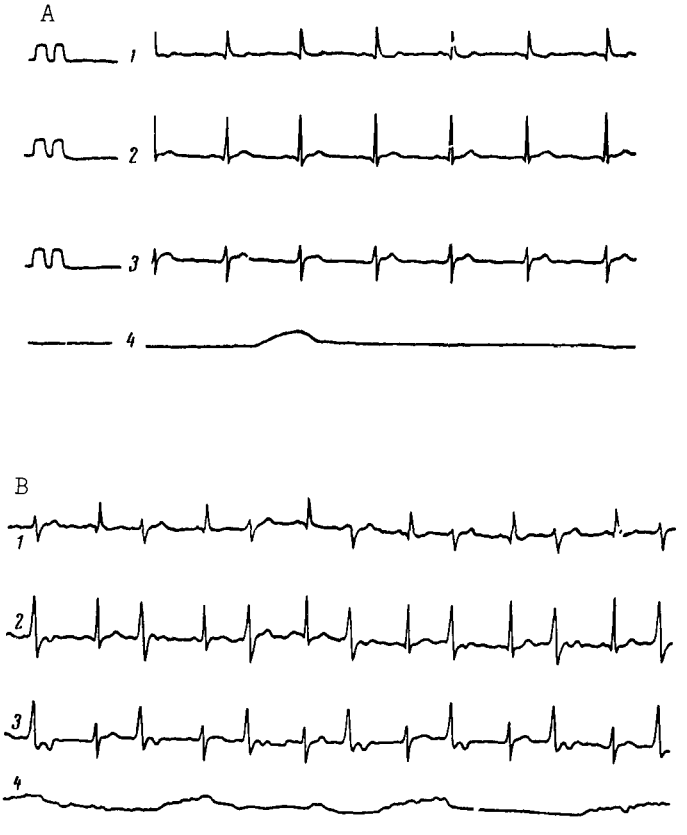

Fig. 1. EKG of Subject P-s Prior to Rotation on the Centrifuge (A) and with a G-load of 10 Units for a Period of 20 Seconds. (B) Background Investigation. Nebu Leads: 1. Posterior; 2 Anterior; 3. Lower; 4. Pneumogram. Running Speed of the Tape

the time of the effect of transverse G-loads have not been completely explained at the present time nor have they been determined, their appearance just as other signs of disruptions in the heart rhythm with the attainment of maximally tolerable G-load values may indicate a relative inefficiency in the coronary blood circulation [8]. It should be noted that F.A. Iordanskaya [10], in studying the adaptation of the heart of athletes to work on a bicycle ergometer after breathing 15% O_2 and 85% nitrogen and after running a distance of 100 m artificially holding the breath, in 13% of the cases the appearance on the EKG of a distinct disruption in the rhythm wasnoted and the form of the extrasystoles was most often ventricular. In carrying out this work but with breathing atmos- /27

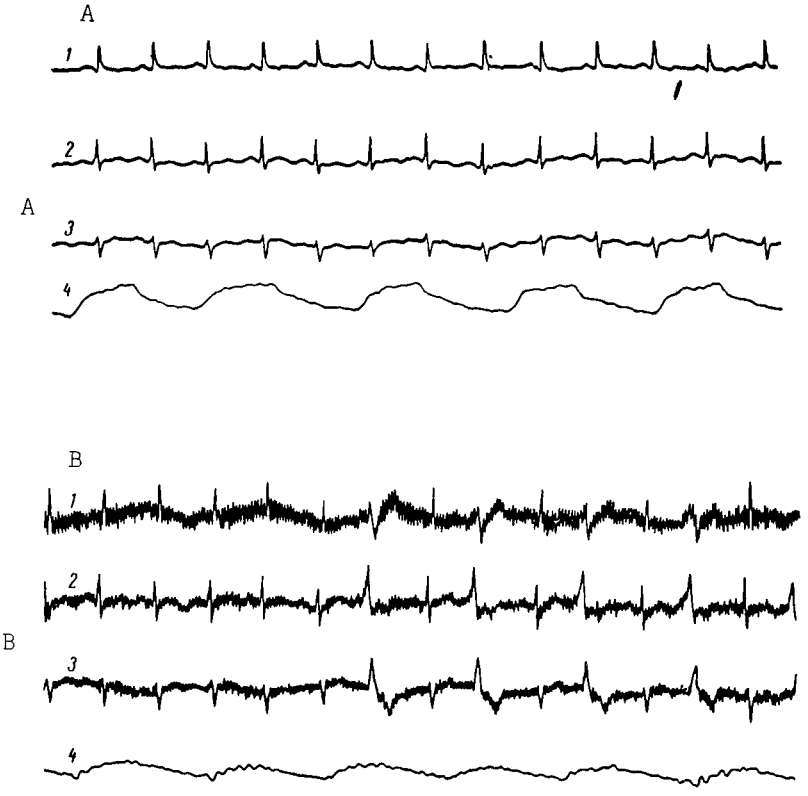

Fig. 2. EKG OF Subject P-s During the Time of a G-Load of 10 Units for a Period of 20 Seconds ("Rest Time"). (A) and With a G-Load of 10-11-12 Units. (B) After Residence Under High-Altitude Conditions. The Other Designations are the Same as in Figure 1.

pheric air, the extrasystole was not recorded in any one of the cases.

Thus the characteristics of changes in the heart function also permit us to assume that active residence under high-altitude conditions when the combined effect of two basic factors, i.e., motive activity and lowered partial oxygen pressure, is accomplished,

facilitated expansion of the functional possibilites of the organism and in the same way guaranteed an increase in its tolerance to the effect of G-loads. /28

Evaluation of the changes in arterial pressure was based on the data of recordings of the systolic pressure in vessels of the arm during the time of the G-load effect and measurements of the blood pressure (after Korotov) prior to and following rotation of the centrifuge. For this purpose we carried out a comparison of the increase in the systolic pressure with identical values of G-loads and also changes in the systolic, diastolic and pulse pressure directly after cessation of the effect before and after adaptation to hypoxia (Table 5).

TABLE 5. CHANGE IS SYSTOLIC PRESSURE IN THE VESSELS OF THE ARM DURING THE TIME OF TH G-LOAD EFFECT WITH A VALUE FROM 7 TO 10 UNITS AND ALSO IN THE PERIOD OF AFTER-EFFECT BEFORE AND AFTER ADAPTATION IN THE MOUNTAINS (MEANS VALUES FOR 15 PERSONS).

Time of the test	Original pressure	Increase during G-load effect	Increase after rotation for 1 min.
Before high altitude	112±9.0	+67±32	+22±9.0
After high altitude	109±10	+68±18	+19±13
Reliability of ifferences	<0.95	<0.95	<0.95

In all cases during the background test at the time of the G-load effect, there were observed changes in the arterial pressure, which are typical of the position of the human body which we chose with respect to the vector of the G-load (angle 25°).

After preliminary adaptation in mountains, no substantial changes from the side of the arterial pressure on the effect of the G-loads was observed. In the period of after-effect in spite of the higher value of the G-load attained after adaptation to hypoxia, arterial pressure in the vessels of the arm also differed slightly from the background values.

Systolic pressure in the vessels of the concha auriculae with increase in the G-load had a tendency to decrease. After adaptation in the mountains the decrease in pressure occurred with G-loads that were greater than during the time of the background test and more often dropped to 40-20 mm Hg.

Comparison of the changes in the systolic pressure in the vessels of the ear and the amplitude of oscillations relative to the identical value of the G-load showed that adaptation in the mountains gives an individually different regional-vascular reaction to the G-load.

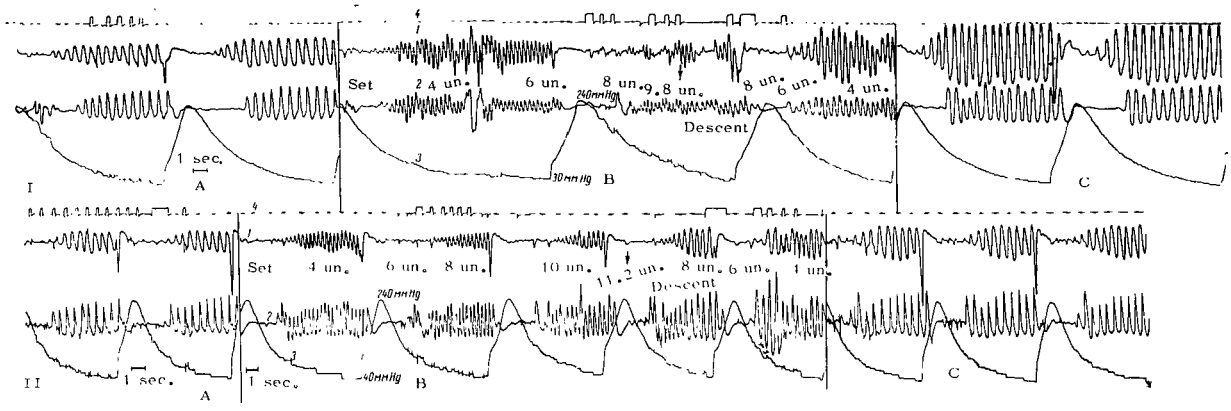

Fig. 3. Arterial Pressure in the Vessels of the Ear and Arm in Subject V-ko Before (I) and After (II) Acclimatization in Mountains. A. Before Rotation; B. During Rotation; C. After Rotation for 1 Min.: 1. Oscillation of Vessels of the Concha auriculae; 2. Oscillations in the Vessels of the Finger; 3. Blood Pressure; 4. Latent Period of the Motive Reaction to Light Signals. /28a

The decrease in the systolic pressures of teh ear following high altitude in the majority of cases was less than during the time of the background tests (Fig. 3). /29

As is obvious from this figure in the background tests with a maximal G-load there was observed a decrease in the amplitude of oscillations of the vessels of the concha auriculae by two times. On the other hand, immediately following rotation the amplitude of the oscillations was increased by more than three times in comparison with the original level. The time of normalization of the arterial pressure was on the average two minutes. After adaptation at high altitudes, in spite of the fact that the effect of the G-loads was greater than the background by 1.4 units, the amplitude of the oscillations in it practically was not lowered but its increase following rotation was also less expressed. The recovery time of the arterial pressure also decreased and was altogether one minute.

Changes in the sign internal breathing with the effect of G-loads prior to and following residence under high-altitude conditions had an identical direction. In connection with the increase in maximally tolerable G-loads following residence in the mountains the signs of breathing were compared with identical G-loads on the segment of the centrifuge acceleration.

The frequency of breathing in proportion to the increase in G-loads gradually increased and the greatest value was obtained at the beginning of slow down of the centrifuge. In the mountain climbers and the subjects who were exposed to high-altitude conditions for the first time, the frequency of breathing under the effect of G-loads on the segment of the acceleration remained approximately at the same level as with the background tests. The difference in the frequency of breathing was not confirmed and consisted on the average of +1.6 and 2.3 of the respiration cycle per minute (with extreme values from -3 to +8 cycles per minute).

On the segment of slow-down the increase in breathing was more sharply expressed than the centrifuge acceleration. After residence under high-altitude conditions the frequency and rate of breathing on this segment of the rotation in the mountain climbers was +2.5 and in the subjects 8.3 cycles per minute in comparison with the original values (Table 6).

The curves of change in pulmonary ventilation and the amount of oxygen required during the effects of G-loads had a two-peak character both before and after conditioning at high altitudes. During the time of "acceleration" approximately up to G-loads of 6.8 units there was observed an increase in pulmonary ventilation and oxygen requirement with a slight increase in the frequency of breathing (Tables 6 and 7). Then in proportion to the increase in G-load the pulmonary ventilation and the oxygen requirements decrease but the frequency of breathing continues to increase.

The second rise in the curve began immediately after lowering the size of the G-load during the time of centrifuge slow-down. In this case there was again noted an increase in the pulmonary ventilation and oxygen requirement (Fig. 4).

Table 7 shows changes in these signs in all subjects before and after residence at high altitude during the period of acceleration of the G-load from 1 - 6 units. With one and the same values of the G-loads after adaptation to hypoxia the pulmonary ventilation in 8 cases out of 11 and the amount of oxygen required in all cases were at a higher level than in the control rotations. With an increase in the threshold of tolerance the pulmonary ventilation increased by 1.8 - 6.8 ℓ/min and the organism's oxygen requirement increased in the different groups to 20-98 mℓ/min. On the other hand, in the subjects (A-v and Ku-s) in whom there was noted a slight decrease in tolerance and ventilation of the lungs, and in A-v the oxygen requirement also at these values of the G-load

/30

TABLE 6. CHANGE IN THE FREQUENCY OF BREATHING (AFTER 1 MIN) WITH THE EFFECT OF TRANSVERSE G-LOADS BEFORE AND AFTER ACCLIMATIZATION IN SUBJECTS AND MOUNTAIN CLIMBERS. /30

Group	Acceleration from 1 to 6 units		Difference	Slowdown from 6 to 1 unit		Difference
	Before acclimatization	After acclimatization		Before acclimatization	After acclimatization	
Subjects						
Al-V	26	25	−1	34	46	+12
Ku-S	21	20	−1	30	35	+5
K-as	12	20	+8	20	44	+24
V-ko	21	24	+3	26	38	+12
Sh-k	22	20	−2	25	27	+2
G-va	19	21	+2	31	34	+3
M-b	22	24	+2	24	29	+5
M ± m	20,4±4,4	22±2,2	+1,6±3,4	27,1±4,8	36,8±7,1	9,0*±7,1
Mountain limbers						
S-t	16	14	−2	22	25	+3
B-n	19	22	+3	42	45	+3
K-b	24	21	−3	30	30	0
N-v	11	13	+2	19	29	+10
B-b	19	25	+6	34	30	−4
Bul-ov	22	29	+7	31	33	+2
G-r	19	21	+3	21	27	+6
M±m	18,6±4,2	20,7±5,7	+2,3±3,6	28,4±8,2	31,3±6,5	+2,9±4,3

*P>0.95.

after high altitude were found to have lower values.

During the period of slowdown of the centrifuge just as during the time of the background rotations there were noted signs of increase in breathing and elevated oxygen requirements as a result of the increased oxygen deficiency in the process of the G-load effect.

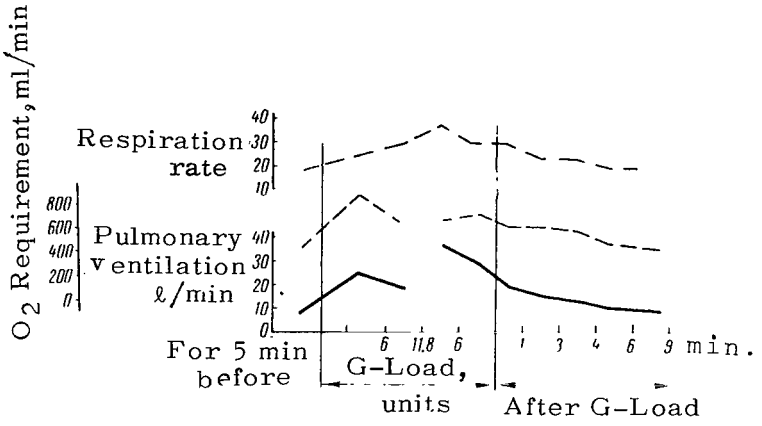

Fig. 4. Character of the Change in Certain Characteristics of Internal Breathing and Gaseous Metabolism Acted on by G-Loads. /31

TABLE 7. CHANGE IN PULMONARY VENTILATION AND OXYGEN REQUIREMENTS DURING THE EFFECT OF TRANSVERSE G-LOADS BEFORE AND AFTER RESIDENCE IN MOUNTAINS FOR THE SUBJECTS AND THE MOUNTAIN CLIMBERS ON THE ACCELERATION SEGMENT.

Group	Difference in G-load tolerance, Units	Acceleration from 1-6 units: Pulmonary ventilation l/min			Acceleration from 1-6 units: O_2, ml/min		
		Before adaptation	After adaptation	Difference	Before adaptation	After adaptation	Difference
Mountain climbers							
S-t	+1,3	10,2	14,4	+4,2	312	380	+68
B-n	+1,9	12,4	19,2	+6,8	—	—	—
K-v	+1,0	12,2	14,4	+2,2	356	410	+54
N-v	+1,8	12,2	12,2	0	372	396	+24
Aver. data		11,8	15,0	+3,2	346,6	395,3	+48,7
Subjects							
A-v	−0,3	21,4	12,2	−9,2	460	396	−64
Ku-s	−0,6	12,5	10,8	−1,7	360	364	+4
Sh-k	+1,2	9,6	11,4	+1,8	302	322	+20
K-as	+3,8	10,2	14,4	+4,2	342	440	+98
Aver. data		13,4	12,2	−1,2	366	380,5	+14,5

Comment: In the subject A-v under high-altitude conditions there were noted signs of altitude sickness. Statistical analysis was not carried out in view of the small number of cases.

After conditioning at high altitudes the degree of these changes was individually different. /32

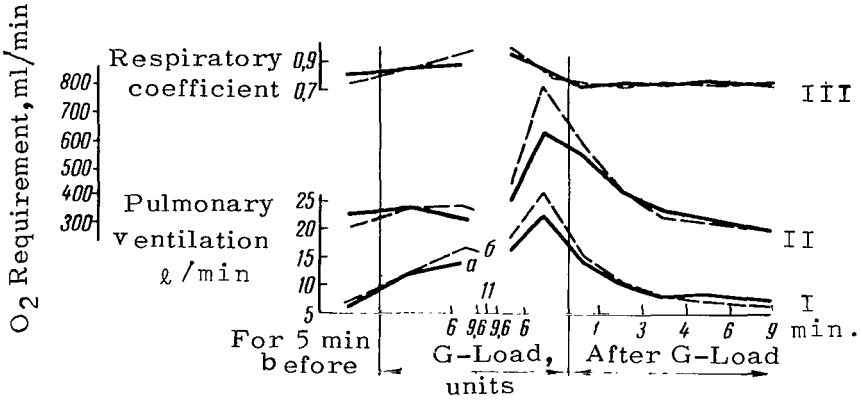

Fig. 5. Change in the Characteristics of Internal Breathing and Gaseous Metabolism in Subject N-va Under the Effect of G-Loads Before (a) and After (b) Acclimatization at High Altitudes. I. Pulmonary Ventilation, l/min; II. Oxygen Requirement, ml/min; III. Respiratory Coefficient.

With the significant increase in tolerance to G-loads (+1.9, +3.8 units) changes in the characteristics of breathing, which characterize the end of oxygen debt, were more sharply expressed (K-as, B-n).

Pulmonary ventilation on this segment of rotation following conditioning at high altitudes in practically all of the subjects (other than K-usa) was found to be higher then during the background tests (Table 8, Fig. 5).

The difference in oxygen requirements with slow down of the centrifuge in all subjects was on the average +38.

In subjects in whom the tolerance to G-loads after adaptation to high-altitude conditions practically did not change or was even lowered somewhat, the oxygen requirement was at a lower level than during the background tests. In one case (K-as) with a significant increase in tolerance to G-loads by +3.8 units the increase in oxygen requirement was most sharply expressed and consisted of 378 ml/min.

As far as the oxygen debt is concerned, which is computed from the moment of startup of the centrifuge until it is stopped, following conditioning at high altitudes in the majority of cases it was less than after the background test or exceeded it only insignificnatly (Table 8).

In only two cases with the largest increase in tolerance (by 1.9 and 3.8 units) the oxygen debt was significantly increased in comparison with the original values (by 501 and 738 ml/min).

TABLE 8. CHANGE IN PULMONARY VENTILATION AND OXYGEN REQUIREMENT ACTED ON BY TRANSVERSE G-LOADS BEFORE AND AFTER RESIDENCE IN MOUNTAINS (ON THE SEGMENT OF SLOW DOWN ON THE CENTRIFUGE). /33

Group	Difference in G-load tolerance, units	Slowdown from 6 to 1 unit						Oxygen debt, ml**		
		Pulmonary ventilation l/min			O_2 Requirement, ml/min					
		Before adaptation	After adaptation on the 10-15 day	Difference	Before adaptation	After adaptation on the 10-15 day	Difference	Before adaptation	After adaptation on the 10-15 day	Difference
Mountain limbers										
S-t	+1,3	15,4	18,0	+2,6	423	420	−3	186	122	−64
B-n	+1,9	27,4	39,5	+12,1	440	450	+10	331	832	+501
K-v	+1,0	21,9	27,0	+5,1	555	545	−10	393	402	+9
N-v	+1,8	22,0	26,7	+4,7	656	810	+154	417	516	+99
Average Data		21,7	27,8	+6,1	518	531	+38	332	463	+136
Subjects										
A-v*	−0,3	29,0	32,5	+3,5	580	525	−55	701	310	−391
Ku-s	−0,6	19,2	18,0	−1,2	398	358	−40	197	0	−197
Sh-k	+1,2	13,0	16,7	+3,7	390	410	+20	37	87	+50
K-as	+3,8	15,8	50,7	+34,9	397	775	+378	0	738	+738
Average Data		19,2	29,5	+10,3	441	518	77	234	284	+50

* Signs of altitude sickness were noted in A-v under high-altitude conditions.

** The oxygen debt was computed from the moment of stoppage of the centrifuge.

The emission of carbon dioxide on the segment of slowdown during the first moments of the aftereffect in all cases was found to be considerably greater than in the background test. On the average the emission of CO_2 on the segment of slowdown (from 6 to 1 unit) consisted of 600 ml/min with 380 ml/min in the control.

Analogous changes were noted also for the size of the respirational coefficient which, following residence at high altitudes retained higher values than in control rotations. In the period of centrifuge slowdown following return from high altitudes the respirational coefficient was equal to 1.16-1.22 with 0.87-0.91 during the time of the background tests. The recovery time of the frequency of breathing in the majority of cases differs very little from the original. Ending of the oxygen debt, the excess amount of carbon dioxide and also the recovery of the respirational coefficient continued as a rule somewhat longer than following the background rotations.

Thus changes in the signs of the internal breathing with the /34
effect of G-loads after adaptation to high-altitude conditions though being identical in direction, had a different appearance. After residence in the mountains with respect to the segment of accelleration of the centrifuge the breathing was more effective than with respective G-loads during the time of the background rotation. The increase in the respirational volume, the amount of the organism's requirement without a noticeable increase in the frequency of breathing should obviously be assumed to be the optical reaction of the onset of adaptation mechanisms in response to anincreased oxygen requirement of the organism acted on by transversely directed G-loads.

Simultaneously with an increase in the oxygen requirement acted on by the G-loads following conditioning to high altitudes there was observed an increase in the respirational coefficient which could be associated with the increasing possibilities of the organism in the elevated utilization of oxygen. On the segment of slowdown following attainment of the maximally tolerable G-load which in the majority of cases was found to be considerably higher than the original, changes in the signs of internal breathing were better expressed. However, the oxygen debt in the overwhelming majority of cases remained at the same or even at a slightly lower level than the background tests.

Thus the physiological changes which characterize the function of internal breathing during the time of the action of transverse G-loads after preliminary residence at high-altitude conditions in a majority of cases should be evaluated as being more optimal in comparison with the background tests.

Analogous changes were found by investigators who studied the function of breathing acted on by physical loads of a static nature [6].

Evaluation of the functional condition of the central nervous

system was based on data of the latent period of the response-motive reaction to light signals and the electroencephalogram. Comparison of the duration of the latent period of the motive reaction was carried out only with an identical value of the G-load. Analysis of the data showed that with increase in the time of the latent period which is characteristic for the effect of transverse G-loads [13], was found to be less after conditioning at high altitudes only in 5 subjects out of the 14 (mountain climbers S-t, B-n, V-ov, and subjects Sh-k, V-ko).

It is interesting that in three of these subjects acted on by identical G-loads the regional blood circulation in the vessels of the concha auriculae were found to be more effective after acclimatization at high altitudes.

Table 9 gives the latent period of the response-motive reaction acted on by a G-load in mountain climber S-t who showed an improvement in the reaction to light following acclimatization.

TABLE 9. LATENT PERIOD OF THE RESPONSE-MOTIVE REACTION TO LIGHT SIGNALS IN MOUNTAIN CLIMBER S-ta. /35

Moment of Investigation	Before residence at high altitude			After					
				10 days			1 month		
	1	2	3	1	2	3	1	2	3
Prior to rotation for 1 min...	0.2	0.2	0.6	0.2	0.3	0.3	0.3	0.2	0.6
With acceleration of the G-load to a level of 5 units.....	0.3	0.3	0.4	0.4	0.4	0.6	0.3	0.5	0.5
With acceleration of the G-load to a level of 9 units.....	No response			0.4	0.4	0.3	0.4	0.4	No Response

1. Central Signal; 2. middle 3. peripheral.

In the other nine cases and also in all cases after conditioning in a pressure chamber, no reliable changes were obtained.

Evaluation of the bioelectric activity of the cerebral cortex acted on by G-loads before and after adaptation at high altitudes was carried out in four subjects. Here in all cases there were observed typical changes in the EEG which are characteristic for the effect of transverse G-loads described by other authors [11, 13, 18]. Before and during the test in the centrifuge, as a rule, there was noted a desynchronization of the cortical rhythms which gradually increased in proportion to the increase in the G-load (phase I of the EEG changes).

During the period of the aftereffect there was an increase in the amplitude of the α-rhythm, a decrease in its frequency and sometimes the onset of individual θ-waves. The period of recovery of changes characteristic for phase II consisted of 3-10 minutes. Comparison of the results of the investigations on the EEG in all the subjects acted on by the G-load did not show any substantial difference after adaptation to hypoxia under high-altitude conditions in comparison with the original data. The period of recovery of the EEG characteristics after the effect of the G-load also did not change. Thus, according to the EEG data, it was not possible to detect specific signs which indicated the appearance of adaptation to hypoxia.

Comparisons of the reactions from the side of a number of physiological systems of the organism at identical levels of the G-load before and after adaptation to hypoxia in our experiments permitted us to show several characteristics of the mechanisms of adaptations to G-loads. These characteristics included amplification of the compensatory reactions of the adapted organism to the G-load which was created in the large increase in rhythm of the heart contractions, the increase in the pulmonary ventilation at /36
the expense of the respirational volume, by the large oxygen requirement during the period of growth of the G-load, by the more significant increase in the systolic pressure in the vessels of the cochlea auriculae.

Increase in the duration of the cardiovascular and the respirational systems in response to the G-load after residence in the mountains most probably should be considered as an adaptation reaction of the organism of man in connection with the increase in utilization of oxygen in the tissues.

On the other hand, there are literature data which indicate an increase in the number of erythrocytes in the hemoglobin and also an increase in the concentration of white blood cells in the plasma of the blood after short-term residence at high altitudes [3, 14, 15, 19].

In our investigations, in the majority of subjects during the time of residence under conditions of high altitude, there was also observed an increase in the number of erythrocytes in the hemoglobin. Here we found substantial differences in the degree of manifestation of the changes in the blood system in different subjects (Y.P. Blagovestova, N.A. Roshchina et al, see this collection, p. 158 of the Russian text, p. 173 of the translation).

According to the data of these authors, in the majority of mountain climbers who participated in our experiments, residence at high altitudes at an altitude of 2000 meters with periodic ascent to altitudes up to 4500 meters did not lead to any substantial changes in the amount of hemoglobin and the number of erythrocytes but in those subjects who were exposed to high altitude for the first

time after 4-5 days there was clearly expressed an increase in the hemoglobin and the erythrocytes which were then found to be in direct dependence on the altitude of the ascent. These data show that the threshold of reaction and the expression are determined to a significant degree by the functional state of the organism. In subjects who in the past had been adapted multiply under high-altitude conditions, the threshold of the reaction which determines the increase in the peripheral blood of the number of erythrocytes and the hemoglobin probably was higher than in those persons who had not been previously adapted to hypoxia. Therefore, obviously, adaptation to hypoxia at relatively low altitudes (2000-4000 m) in mountain climbers occurs due to other functional systems, namely, due to breathing and blood circulation.

For a better understanding of the mechanisms of adaptation of an organism to the effect of G-loads after preliminary adaptation to hypoxia we thought it would be interesting and important to analyze the obtained data according to the tolerance of G-loads with changes in the blood system.

The analytical data showed that no strict correlation between the character and the size of the changes from the site of the blood in the process of adaptation to altitude and the subsequent tolerance of the subjects to the effect of G-loads was detected. Changes in the blood system noted under high-altitude conditions after return to Moscow in the majority of cases during the period of the next 5-12 days was laready absent.

Comparison of the number of erythrocytes and the amount of /37
hemoglobin directly after rotation in the centrifuge with the tolerance of G-loads showed that the no reliable correlation was noted (Table 10).

Out of the ten cases, in two of the subjects there was noted a significant increase in the number of erythrocytes and the hemoglobin before rotation and an increase in the tolerance to G-loads; in three of the subjects there were no changes in the blood system and the tolerance of the G-loads increased; in one of the subjects significant changes in the tolerance to G-loads and the blood characteristics were lacking; in the other cases the taking of the blood analyses did not correspond in time with the rotation in the centrifuge. However, based on the dynamics of recovery of the blood characteristics in the latter group of subjects, we may assume that at the moment of rotation on the centrifuge, i.e., on the 10th-15th day following descent to the plain, the amount of hemoglobin and the erythrocytes was already near the original values. Thus the impression is created that among the mechanisms of adaptation of an organism to the effect of G-loads after preliminary residence under high-altitude conditions the blood system obviously is not a basic factor which leads to expansion of the functional possibilities of the organism. However, the lack of a sufficient amount of data concerning the changes in the blood system directly before the tests on the cen-

TABLE 10. COMPARISON OF THE TOLERANCE TO G-LOADS AND CHANGES OF THE BLOOD SYSTEM (SELECTED DATA).*

Subject	Time of rotation on the centrifuge**, days	Difference in G-load tolerance, units	Erythrocytes			Hemoglobin		
			Before high altitude	After high altitude		Before high altitude	After high altitude	
				On the 5th day	On the 12th day		On the 5th day	On the 12th day
Sh-k	12	+1.2	5.2	-	5.3	15.4	-	17.1
G-r	12	+2.8	4.9	5.4	5.2	14.6	16.3	15.4
V-ko	10	+1.4	5.1	5.1	-	14.3	14.5	-
Ku-s	11	-0.6	5.7	5.5	-	17.5	17.4	-

* The table has been compiled according to the data of N.P. Blagovestova and N.A. Roshchina.
** The time of rotation on the centrifuge and taking of the blood was computed from the moment of descent of the subjects from the mountain to the plain.

rifuge after residence under high-altitude conditions makes it necessary to carry out additional investigations in this direction.

Basic attention is paid in studying the process of adaptation to reactions from the side of the vessels of the brain. According to the data of several authors [3, 7, 9], in the process of adaptation /38 to chronic hypoxia the blood circulation inside the brain is increased. In fact, according to the data of V.V. Barin, N.A. Agadzhanyan, A.S. Barer, et al, [17], an improvement was noted in the blood circulation of the brain acted on by transversely directed G-loads with a value of 8-10 units in all of the subjects following a 45-day residence at high altitudes. Therefore, the distinct improvement in the function of visual perception observed in our experiments during the time of G-load effect was possibly associated with improvement in the blood circulation inside the brain and also with an increase in the tolerance of the neurons of the retina to hypoxia. This latter discussion has been confirmed by indirect experimental data. In particular, as many investigators have shown [1, 4, 12, 20, 21, 22], the tissue adaptation during chronic hypoxia may be developed in two directions: due to the amplification in the oxidation processes with lowering of the partial oxygen pressure as a result of increasing the amount of myglobin, cytochrome C and other oxidizing ferments, and also the increase inthe processes of anaerobic glycolysis including the cells of the central nervous system.

Z.I. Barbashova [4] in her investigations noted a direct correlation between the tolerance of the entire organism and the resistance of its tissues. In particular in rats with an increased tolerance

of the complete organism the resistance of the myocardium and the skeletal muscles were found to be greater, as well as the tissues of the brain, and in particular the cells of the respirational and the vasomotorial centers. In studying several of the biochemical processes it was found that these tissues possess the ability for a more active utilization of oxygen from the environment which is stongly depleted of oxygen.

Thus the investigations which we carried out showed that residence under high-altitude conditions facilitated expansion of the functional possibilities of the organism which guaranteed a significant increase in its tolerance to the effect of transversely directed G-loads.

The increase in the adaptation possibilities of the organism to the effect of G-loads after preliminary residence under high-altitude conditions came about as a result of the combined effect of two of the basic factors: the motor activity and the lowered partial oxygen pressure.

The most important pathogenetic mechanism of increase in the adaptation possibilities of the organism to G-loads after residence under high-altitude conditions should probably be considered as the increase in the activity of the functional systems of breathing and blood circulation and also changes in the cellular chemism which are the essence of the process of adaptation to hypoxia. As far as the changes in the blood system are concerned, probably they do not have in this case a determining significance. However, investigations of the mechanisms of adaptation must be not only carried out but also /39 expanded since their study has significant theoretical and important practical significance.

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THE EFFECT OF ADAPTATION TO HYPOXIA UNDER PRESSURE-CHAMBER CONDITIONS ON TOLERANCE TO TRANSVERSE G-LOADS

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ABSTRACT: The effect of intermittent conditioning to hypoxia was studied in a pressure chamber on the tolerance of man to transverse G-loads. The conditioning was carried out by successive ascents every 3-7 days to altitudes of 4000 to 7000 m with rest periods at each altitude for 30 minutes. The duration of the training schedule was 20-25 days. It was established that after pressure-chamber conditioning an increase is noted in tolerance to G-loads, which on the average is +1.35. The increase in tolerance to G-loads after conditioning in a pressure chamber was less than after high-altitude training. The authors propose that adaptation to hypoxia may be used for purposes of pre-flight training and for increasing tolerance of the astronaut during prolonged flight before returning to Earth.

The research of many Russian and foreign investigators has established that prolonged adaptation to high-altitude conditions is one of the effective means of increasing tolerance of an organism to the effect of various adverse environmental factors (acute hypoxia, variations in temperature, radiation, etc.). Adaptation to oxygen deficiency under pressure-chamber conditions has been proposed some time ago by Russian investigators for increasing tolerance of an organism to the effect of acute hypoxia. Many investigators, in studying the mechanisms of adaptation of the human organism to high altitude, have shown that the acclimatization effect is reached only after many ascents or after many hours of remaining at high altitude [1, 5, 7-12]. /40

In the research conducted by Klein, Brüner and Jovy [13, 14] it was shown that, when man remained under high-altitude conditions, the reactions of his physiological systems are considerably improved in regard to the effect of positive G-loads due to the involvement of nonspecific mechanisms. The increase in tolerance to transversely directed G-loads was also established in experiments on animals who were adapted to conditions of hypoxia [3, 4].

We previously found an analogous effect on persons exposed to high-altitude conditions and who have shown a distinct increase in tolerance toward the effect of transversely directed G-loads [2, 3].

The results of these investigations permitted us to assume that acclimatization in mountains is one of the effective methods of nonspecific conditioning and the duration of retention of this positive effect of adaptation showed the feasibility of using this method for pre-flight training of astronauts. It is known that the oxygen factor has a definite significance in the reactions of an organism at high altitude and there are quite similar characteristics in the adaptation of an organism to pressure-chamber and high-altitude hypoxia. At the same time the method of adaptation to hypoxia under pressure-chamber conditions differs essentially as compared to acclimatization in mountains. First of all, the use of such a method is independent of seasonal variations in climate and geographical location. Secondly, adaptation to hypoxia in this case may be carried out not only in the conditioning period but also during space flight. Thirdly, it is possible to make a strict quantitative evaluation of the various effective conditions for choosing the optimal /41
one. Based on these arguments we felt that it was feasible to determine the possibility of increasing man's tolerance to the effect of G-loads after having been previously adapted to hypoxia under pressure-chamber conditions.

The investigations were carried out on four subjects who had not been previously subjected to high-altitude adaptation. Prior to conditioning in the pressure chamber, tolerance to the effect of extreme maximally endurable G-loads was determined on each of them. Endurance to G-loads was studied in a centrifuge in all cases from at least two background experiments and once (after 1-4 days) following completion of conditioning in the pressure chamber. The method used to find the limit of tolerance and registration of the physiological parameters has been discussed in previous papers (see the present collection, original pp. 7 and 17).

Pressure-chamber conditioning was conducted intermittently by successive ascents to altitudes of 4000, 5000, 5500, 6000, 6500 and 7000 m every 3-7 days. The duration of residence at each altitude was 30 minutes. The rate of ascent in the pressure chamber was equal to 25 m/sec. The duration of the entire training cycle in the pressure chamber was 20-25 days. Prior to and after conditioning, tolerance to oxygen starvation (altitude-ceiling) was determined.

For the purpose of improving respiration, the subjects were first instructed in a voluntary increase in breathing intensity while retaining the usual frequency recommended at "altitudes" above 4000 m.

In compiling data from the training schedule in the pressure chamber, the results of the investigations carried out by Vasil'yev

and Uglovaya [3] on animals, as well as the high effectiveness of intermittent conditioning in a pressure chamber, were taken into account. Here the authors showed that the increase in tolerance of animals to G-loads after intermittent and continuous conditioning in the pressure chamber was practically the same.

The results of the investigations showed that in all four subjects, after pressure-chamber conditioning, an increase was noted in their tolerance to transverse G-loads that was, on the average, +1.35 $\pm$ 0.8 (Table 1).

Individual improvements in tolerance were associated in all cases with an increase in the threshold of the onset of optical disorders and varied in a range from +0.7 to +2.5 (see the figure).

According to data from the subject's response, in three cases out of four the subjects noted an improved tolerance to G-loads after pressure-chamber conditioning. This was expressed in the easier breathing and the sensation of pressure on the chest, and by the delayed onset of optical disorders. Visual acuity, determined at different average values of the G-load with acceleration of the centrifuge, in all cases after pressure-chamber conditioning was found to be higher than with the background tests (Table 2). Thus, a corrolation was found between the improvements in the threshold of onset of optical disorders and visual acuity produced by the effect of G-load after preliminary conditioning in a pressure chamber. /42

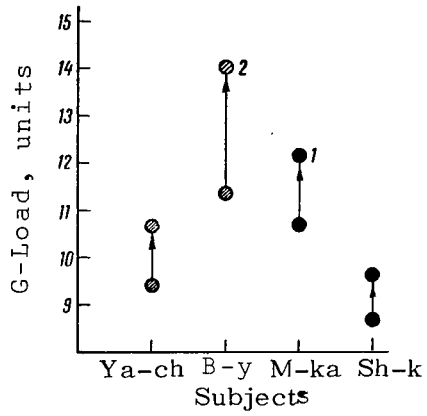
TABLE 1. CHANGE IN G-LOAD TOLERANCE AFTER PRESSURE-CHAMBER CONDITIONING

Subject	Before Conditioning	After Conditioning	Difference	Tolerance criteria
Ya-ch	9.5	10.5	+1.0	"Gray Veil"
B-y	11.5	14.0	+2.5	" "
M-ka	10.8	12.0	+1.2	"Black Veil"
Sh-k	8.8	9.5	+0.7	" "
Average	10.1 $\pm$ 1.2	11.5 $\pm$ 1.9	+1.35 $\pm$ 0.8	" "
Reliability of differences	—	—	>0.95	" "

It was interesting to compare the improvements in G-load tolerance and to acute oxygen starvation after multiple times in the pressure chamber (Table 3).

It was established that following pressure-chamber conditioning the altitude ceiling in two of the subjects increased to 1000 m, in the two others it did not change. The time of residence at high altitude was increased in three of the persons. Comparison of the individual tolerance to acute oxygen starvation and G-load revealed

similar characteristics. It was shown that in one of the subjects (Sh-k) in whom no change was noted in altitude resistance the G-load tolerance changed also very little; in two of the others an increase in altitude ceiling and threshold of G-load tolerance was observed. Here the greatest increase in G-load tolerance (+2.5) was found to be in that subject (B-y) in whom the greatest increase in altitude tolerance was also noted. /43



Change in the Level of G-Load Tolerance and Characteristics of Optical Disorders in Four Subjects After Pressure-Chamber Conditioning. 1. "Black Veil"; 2. "Gray Veil". The Arrow Shows the Direction of Improvement Following the Pressure Chamber.

Thus the results of change in altitude tolerance after repeated exposure in a pressure chamber, to a known degree, permits us to predict the change in G-load tolerance.

Of considerable significance for showing the possible mechanisms of nonspecific adaptation is the investigation of the characteristics of physiological reactions to a G-load in persons who have been adapted to hypoxia.

Of greatest interest in this respect are the results of investigations of the cardiovascular system, the systems of breathing and gaseous metabolism. For this purpose we have analyzed

TABLE 2. CHANGE IN VISUAL ACUITY UNDER THE INFLUENCE OF G-LOADS PRIOR TO AND AFTER ADAPTATION IN A PRESSURE CHAMBER.

Subject	Improvement in Threshold of Onset of Arterial Disturbances, Units	Before Adaptation Pressure Chamber		After Adaptation in Pressure Chamber	
		G-Load, Units	Visual Accuity	G-Load, Units	Visual Accuity
Sh-k . . .	+0,7	6,0—8,0	0,4	6,5—8,5	0,6
M-ka . . .	+1,2	7,5—9,1	0,3	7,5—9,5	0,4
B-y . . .	+2,5	9,0—11,0	0,5	9,0—11,0	1,0
Ya-ch . .	+1,0	7,0—9,0	0,5	8—10,0	0,5

Comment: The values of the G-load for which visual acuity was determined in the subjects are indicated.

TABLE 3. CHANGE IN ALTITUDE TOLERANCE PRIOR TO AND AFTER REPEATED EXPOSURE IN A PRESSURE CHAMBER.

Subject	Altitude Ceiling		Improvement in G-Load Tolerance, units
	Before Conditioning	After Conditioning	
Ya-ch	7 km—2 min	7 km—3 min	+1.0
B-y	7 » —1 »	8 » —3 »	+2.5
M-ka.	7 » —2 »	8 » —2 »	+1.2
Sh-k	8 » —1	8 » —1 »	+0.7

and compared the physiological improvement recorded during the action of G-loads which are identical in value prior to and after pressure-chamber conditioning. The functional state of the cardiovascular system was evaluated for all subjects based on readings of the pulse rate and the breathing rate, of an EKG in three Nebo leads, systolic pressure in the vessels of the humerus and the cochlea, based on recovery time of the physiological functions. /44

TABLE 4. CHANGE IN PULSE RATE AND BREATHING RATE DURING THE ACTION OF G-LOADS OF 8-9 UNITS PRIOR TO AND AFTER PRESSURE-CHAMBER CONDITIONING.

Subject	Improvement in G-Load Tolerance, Units	Before Conditioning		After Conditioning		Difference	
		Pulse rate beat/min	Respiration rate	Pulse rate beat/min	Respiration rate	Pulse rate beat/min	Respiration rate
Sh-k .	+0.7	102	27	102	27	0	0
M-ka .	+1.2	103	21	114	23	+6	+2
B-y . .	+2.5	107	24	109	23	+2	+2
Ya-ch	+1.0	126	24	126	30	0	+6

In all cases changes were noted in the cardiovascular readings which are characteristic of G-load effect and have already been described in a previous article. No substantial difference could be detected in the improvements in these characteristics prior to and after pressure-chamber conditioning (Table 4).

After conditioning under pressure-chamber conditions, the improvements in the electrocardiograph readings in one of the subjects was the same as with background tests; in the other three, they had individual characteristics. Thus, in the subject M-ka at the time of the background tests when the centrifuge was accelerated at a G-load of 10.8, signs of relative bradycardia were noted with

the reduction of R-R from 0.59 to 0.70 sec. After conditioning in a pressure chamber, analogous disruptions in rhythm were observed during the action of G-loads with a value of 12. In the other subjects with background rotation tests a slight non-conformity was noted in the length of the interval Q-T and R-R; the relative duration of the electrical systole was 120-130% [15]. After training /45
in a pressure chamber the EKG of these subjects acted on by large G-forces was without characteristics and the relative length of the electric systole corresponded to the frequency of the rhythm. We may assume that these improvements indicate an increase in the functional capacity of the heart muscle after adaptation to hypoxia.

TABLE 5. RECOVERY TIME OF BLOOD PRESSURE (SYSTOLIC AND DYASTOLIC) IN THE PERIOD OF AFTER-EFFECT OF THE G-LOAD PRIOR TO AND AFTER CONDITIONING IN A PRESSURE CHAMBER.

Subject	Increase in G-Load Tolerance, Units	Time, min.			Subject	Increase in G-Load Tolerance, units	Time, min.		
		Before Conditioning	After Conditioning	Difference			Before Conditioning	After Conditioning	Difference
Ya-ch	+1.0	6	2	-4	Ya-ch	+1.2	5	1	-4
B-y	+2.5	6	4	-4	B-y	+0.7	6	2	-4

TABLE 6. CHANGE IN THE AMPLITUDE OF OSCILLATIONS OF VESSELS OF THE COCHLEA ACTED ON BY G-LOADS PRIOR TO AND AFTER CONDITIONING IN A PRESSURE CHAMBER (DIFFERENCE IN % OF THE ORIGINAL VALUE).

Subject	Before Pressure Chamber Conditioning		After Pressure Chamber Conditioning	
	G-Load, units	Difference, %	G-Load, units	Difference, %
Ya-ch. .	9	— 50	9	—20
M-ka . .	11	- - 50	11	—50
B-y . . .	8	- - 10	8	—10
Sh-k . .	6	-100	7	—50

Comment: These G-loads correspond to the period of centrifuge acceleration.

The recovery time of blood pressure in the vessels of the humerus and the period of after-effect of the G-load following previous adaptation in a pressure chamber was found in all cases to be shorter than in the background tests in spite of the high value of the G-load attained (Table 5).

The amplitude of oscillations of the cochlea vessels acted on by G-loads had a tendency to be lower. After conditioning in a

pressure chamber these improvements in two instances were considerably less than with background test, in two others no difference was noted (Table 6). /46

Pulmonary ventilation and the requirements for oxygen in all background tests gradually increased in proportion to the increase in G-loads. Under the action of a G-load that is extreme in value, as a rule there was noted a decrease in the respiratory volume and pulmonary ventilation with a sufficiently high frequency of breathing. When the centrifuge was slowed down, the increase in pulmonary ventilation and the O_2 requirement was the greatest. After conditioning under pressure-chamber conditions the double-peak type of curves which characterized pulmonary ventilation and O_2 requirements did not change. However, qualitative improvements were noted. When the centrifuge was accelerated from 1 to 6 after adaptation to altitude, the increase in pulmonary ventilation and oxygen requirements were found to be more significant than in the background tests (Table 7).

TABLE 7. CHANGE IN PULMONARY VENTILATION AND OXYGEN REQUIREMENTS DURING THE ACTION OF TRANSVERSE G-LOADS PRIOR TO AND AFTER PRESSURE-CHAMBER CONDITIONING.

Subject	Difference in G-Load Tolerance, units	Pulmonary Ventilation, l/min			O_2 Requirement, ml/min			Oxygen Debt		
		Before Conditioning	After Conditioning	Difference	Before Conditioning	After Conditioning	Difference	Before Conditioning	After Conditioning	Difference
Ya-ch	+1,0	15,8 *	17,3	+1,5	380	420	+40			
		23,0 **	23,4	+0,4	512	550	+38	730	269	—461
M-ka	+1,2	9,6 *	11,5	+1,9	351	392	+41			
		14,1 *	14,2	+0,1	305	368	+63	0	0	0
Sh-k	+0,7	9,6 *	10,8	+1,2	302	310	+ 8			
		13,0 **	17,4	+4,4	390	430	+40	37	61	+24

* When the centrifuge is accelerated from 1 to 6.
** When the centrifuge is slowed down from 6 to 1.

It follows from Table 7 that the increase in pulmonary ventilation and O_2 requirements when the centrifuge slows down after adaptation to high altitudes is obviously due to the decrease in the oxygen debt during the effect of G-loads in spite of the fact that the size of the effect was 1-1.2 greater in comparison with the background investigation. In one case (Sh-k), where after conditioning in the pressure chamber an increase was observed in the oxygen debt, the increase in G-load tolerance was found to be the least.

The obtained data indicate an increase in the effectiveness of /47
the operational system of external respiration after pressure-chamber conditioning when the centrifuge is accelerated.

The change in the characteristics of external respiration and gaseous metabolism after pressure-chamber conditioning was similar to the improvements in the systems after acclimatization in mountains.

Based on data from the investigation at the time of the motor response reaction to light and the EEG in all four subjects, no difference was found in the characteristics of the physiological reaction to G-load before and after pressure-chamber conditioning.

Thus the data which we obtained would permit us to assume that repeated ascents in a pressure chamber may be one method for increasing the man's tolerance to the effect of transversely directed G-loads. However, unlike the previous series of experiments carried out under high-altitude conditions, in this case only one of the basic factors, i.e., the lowered partial pressure of oxygen, facilitated discovery of compensatory mechanisms which aid in improved G-load tolerance. The passive residence of subjects at high altitudes under pressure-chamber conditions prevented any effect from the other important factor, i.e., motor activity which, in conjunction with hypoxia, would probably guarantee a greater increase in the functional reserve. The obtained data show that improvements in tolerance after high-altitude acclimatization were on the average found to be somewhat higher than after pressure-chamber conditioning.

This difference is also explained apparently by the considerable muscular activity under high-altitude conditions.

In the investigations by Vasil'yev et al. [3] on animals, the high effectiveness was distinctly shown in this respect of active acclimatization in comparison with passive acclimatization. There is no doubt that the characteristics of a mountainous climate, such as temperature of the air, solar radiation, ionization, etc., have distinct significance for developing the processes of nonspecific adaptation. However, they play a secondary role. Based on these discussions we may assume that multiple ascents in a pressure chamber in conjunction with physical training under high-altitude conditions may be still a more effective method of increasing the tolerance of man to the effect of transverse G-loads.

The obtained positive effect of nonspecific influence of hypoxia has great practical significance and may be used both for pre-flight training and for increasing the astronaut's tolerance prior to return to Earth after prolonged flight.

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CHARACTERISTICS OF DEVELOPMENT OF THE ADAPTATION SYNDRONE TO ACUTE HYPOXIA IN MOUNTAIN CLIMBERS

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ABSTRACT: A study was made with 19 highly-qualified mountain climbers and 20 healthy young men as a control group. In all of the subjects the altitude tolerance was determined by gradual "ascent" in a pressure chamber. A greater high-altitude tolerance was found in the mountain climbers in comparison with the control group. Here attention was paid to the fact that in the majority of mountain climbers at high-altitude there was an increase in pulmonary ventilation which was considerably greater than in those comprising the control group. The reaction characteristics of respiration, and the cardiovascular and central nervous systems, in the mountain climbers have been described in the course of ascending to 7000 - 9000 m in the pressure chamber.

The purpose of this paper was to determine the altitude tolerance and to study several sides of the mechanism of adaptation to acute hypoxia of healthy young subjects who had previously been repeatedly subjected to high-altitude conditions. In this connection in the investigation we used the participation of highly qualified mountain climbers who were master athletes and first category subjects who for a period of many years (from 8 to 17) had spent one to two months per year in the mountains. We studied the mountain climbers as subjects who had been adapted to prolonged residence under conditions of lowered barometric pressure. Moreover, we assumed that the mountain climbers could be their own standard toward which we should strive in carrying out altitude conditioning of subjects who had previously not undergone oxygen deficiency for a prolonged period of time. As the control group we used in the research young men who for all practical purposes were healthy but who had never lived under high-altitude conditions. /48

In 19 mountain climbers and 20 subjects from the control group by gradual "ascent" in a pressure chamber we determined the altitude tolerance. The "ascent" was carried out at a rate of 25 m per second with a 20-second rest at each kilometer. From an altitude of 5000 m at each subsequent altitude the duration of the rest period was 5 minutes and at an altitude of 7000 m where the physiological investigations were carried out more completely the duration of residence was 30 minutes. /49

The signal for cessation of the altitude investigation was a sharp decrease in the work capability or a deterioration in the state of being.

The choice of the gradual ascent as a test for determining altitude tolerance was due to the fact that such a methodological approach makes possible a more precise evaluation of the characteristics of the individual tolerance of man to hypoxia since it permits establishing in the process of the "ascent" the threshold changes in breathing, heart activity and other functional systems about which it is extremely difficult, and now and then impossible, to judge in determining the "reserve time", i.e., with a sudden cessation of the oxygen supply at high altitudes.

In the process of the altitude investigation in a-l of the subjects we carried out registration: the EEG in 6 leads, the EKG in 3 standard leads, respirational motions of the chest, saturation of the arterial blood with oxygen and in part of the investigations we determined the partial CO_2 pressure in the alveolar air.

To judge the condition of the work capability by the subjects at various moments of residence at high altitude we proposed mathematical and logical problems, we recorded the state of being and committing to memory of text. The activity of the subjects at high altitude (effectiveness of carrying out one or another assignment) was documented in 15 experiments by moving picture film.

Our first observations in 1958-1959 refer to a group of mountain climbers who entered the USSR in a team. In connection with the then-proposed ascent to Mt. Everest we carried out a determination of the altitude tolerance in 10 of the mountain climbers in the pressure chamber. In this case we were interested in the possibility of retaining work capability at altitudes up to 9000 m under conditions of a different degree of oxygen deficiency. We found that with ascent to an altitude of 5000 m without additional oxygen supply the weight of the hypoxic state in the mountain climbers was considerably less than in subjects of the control group, i.e., those not adapted to high altitude. In the mountain climbers with a relatively insignificant increase in pulse rate the pulmonary ventilation increased to a larger degree than in the subjects of the control group. We noted also that the mountain climbers carrying out physical exercises at an altitude of 5000 m leads to less prolonged and less well-expressed hypoxic changes in the heart activity and breathing.

These observations permitted us to assume that in the process /50
of multiple acclimatization to high altitude in the mountain climbers there is developed a sufficient stationary increase in tolerance to acute hypoxic hypoxia and possibly to certain other extreme factors of the environment.

To prove this assumption and to investigate the characteristics of the physiological mechanism of adaptation to acute hypoxia, we determined the altitude tolerance in 19 mountain climbers directly before going into the mountain, i.e. after 10 months following return from the last mountain-climbing expedition.

We judged the altitude tolerance of the subjects according to the time of residence at high altitude. Of 20 subjects from the control group at an altitude of 7000 m for a period of 30 minutes without oxygen only 3 persons were able to remain. In this case the requirement for oxygen supply at this altitude, for a period of the first 5 to 8 minutes, increased in 10 persons. In 4 of them there was noted a loss in consciousness and deep disruptions of consciousness with the appearance of clonic spasms in their writing hand in five of the subjects and in one a seizure of nausea. Seven of the subjects retained at seven thousand meters a lower level of work capability with relatively clear consciousness for a period of 8 to 20 minutes.

The altitude tolerance was found to be higher than in the control group. Thus of 19 persons, only 2 could not remain for a period of 30 minutes at an altitude of 7000 meters. Here in one of the subjects on the 40th second of residence at an altitude of 7000 meters their cardiac activity suddenly ceased (syncope) with a subsequent deep loss of consciousness and large convulsive seizure. Careful anamnesis and further testing permitted us to establish here the Adams-Stokes syndrome.

In the second subject at the fourth minute of residence at an altitude of 7000 m during the time of writing, in the right hand there appeared sharply expressed clonic spasms, after which he ceased to adequately react to the commands of the experimenter.

The other 17 persons at an altitude of 7000 m retained a relatively high level of work capability for a period of 30 minutes. In this case transient interruptions in handwriting were noted in 7 of the persons in the first 5 minutes of residence at this altitude. In the first 2-3 minutes of residence at an altitude of 8000 m there were observed deep disorders in coordination of motion, clonic spasms of the muscles of the fist of the right hand with retention of relatively clear consciousness. The time for solving the arithmetical and the logical problems increased in them by more than 2 times, in the writing there appeared a perseveration of the individual letters, words and numbers.

Switching over to breathing with pure oxygen after 10-20 seconds led to complete disappearance of the clinical and logical phenomena of the hypoxic state and to recovery of work capability.

Eleven of the subjects for a period of five minutes could remain at an altitude of 8000 m with a satisfactory overall condition. They solved rather complex mathematical problems, completely /51

adequately reacted to commands of the experimenter, and without substantial errors they copied text committed to memory and critically reported on their own condition.

We could judge as to the lowering of the work capability only by the increase in the time needed to solve problems and from the change in handwriting which became more blurred and less structured. In these subjects the deep disorders in the work capabilities were noted on the 1-3 minute of residence at an altitude of 9000 m. These disorders appeared in the majority of cases in the disruption of coordination of motions, spasms in the writing hand or in the development of slow down and sommolence.

Thus, we established substantially higher tolerance to acute hypoxia in mountain climbers than in subjects in the control group. To understand the essence of these phenomena it is of definite interest to compare the reactions of breathing, blood circulation and the central nervous system in mountain climbers and the control group during "ascent" in a pressure chamber.

With decrease in the barometric pressure the increase in the ventilation of different subjects is expressed differently. In the majority of mountain climbers (in 12 out of 19) it was sharply increased. The arbitrary increase in breathing had substantial significance; we judged about this from the fact that when the subject paid attention to describing his state of being conversation and reading, the ventilation substantially decreased.

A sharper increase in the pulmonary ventilation at high altitude in the mountain climbers led to the saturation of the arterial blood with oxygen being higher in them, but the P CO_2 in the alveolar air being lower than in the control group. Thus, the saturation of arterial blood with oxygen at an altitude of 5000 m in the control group was on the average 74%, and in mountain climbers 82%, i.e., 8% greater than in subjects of the control group; at an altitude of 7000 m for 5 minutes it varied from 82-58%, the average was 72%; in the control group the variations were from 48-70, on the average 62%.

Certain differences were detected also in the holding time of breathing at an altitude of normal inspiration, which at 5000 m in the control group was held on an average from 40-23 sec and in the mountain climbers from 70-33 sec. In this case oxyhemometric data showed that the mountain climbers resumed breathing at lower values of oxygen-saturated arterial blood than those of the control group.

As we showed previously [5], with ascent to altitudes of 5000-7000 m, disorder in the rhythm of breathing (periodic breathing) is noted in 25% of the unconditioned subjects. In the mountain climbers no distinct disorders in the breathing rhythm were observed.

With an arbitrary maximally attainable hyperventilation at an altitude of 7000 m there appeared clear hypocapnic changes in the mountain climbers with a lower P CO_2 in the alveolar air than in the control subjects. /52

The increase in the holding time of breathing and the increase in the possibility of carrying out a more intense hyperventilation at high altitudes than with the control group indicates that the range of regulation of breathing in the mountain climbers is significantly greater than in the control group. In analyzing the data from the electrocardiographic investigation we found certain peculiarities in the reaction of the cardiovascular system in the mountain climbers during their "ascent" in a pressure chamber to altitudes of 5000-9000 m. It is known that an increase in the frequency of heart contractions is one of the earliest reactions partial oxygen pressure in the inhaled air. The experiment compiled by the investigators who studied the course of the acute hypoxic state during "ascent" in the pressure chamber [1-4], and also the medical observations on the mountain climbers under the conditions of the high mountain expeditions showed that from the character of the pulse reactions and from the dynamics of its changes it is possible to a known degree to judge as to the adaptation of an organism to the conditions of oxygen deficiency. Thus at an altitude of 5000 m with the same original pulse rate on Earth of 68 beats/minute, in the control subjects the pulse rate was elevated to 85 beats on the average and in the mountain climbers to 82. This small difference increases substantially at higher altitudes, especially with prolonged residence there. Thus, at an altitude of 7000 m by the 10th minute in subjects of the control group the average pulse rate was 96 beats/minute and in the mountain climbers, 86. It is interesting that with this pulse rate in three of the subjects from the control group who remained for 30 minutes at an altitude of 7000 m, at the end of the study it was 107 per minute on the average whereas in the mountain climbers after 25 minutes following "ascent" to 7000 m it was 82 beats/minute on the average. In studying the character of the individual reactions of the pulse reactions, it is clear that in several of the mountain climbers who possess high tolerance to hypoxia in the process of "ascent" a significant indifferent zone was noted, i.e., the first increase in frequency of heart contractions was observed only with the attainment of relatively high altitudes: 5000-6000 m. There were no similar thresholds of change in the pulse rate with the first "ascent" to high altitude of the control subjects. Such a pulse reaction was observed by us only in several of the especially altitude-tolerant subjects after brief, repeated "ascents" to altitudes of 5000-7000 m.

Both in the control group and in teh mountain climbers there occurred similar changes in the value, the shape of the EKG waves and the duration of the individual intervals. They were manifested in a decrease in the value of the R_2 and R_3 waves and by a relatively small decrease in R_1. Here in several of the subjects an increase /53

in the S_2 and S_3 waves was also noted. These changes were caused both by the development of a position levogram and by the effect of the hypoxemia itself.

In almost all of the subjects we noted to a greater or smaller degree a distinct flattening of the T waves in all leads. In 50% of the subjects we noted an increase in the P_2 and P_3 waves; here the P_1 had a tendency to be lowered or was not substantially changed.

The time of conducting the stimulation from the atrium cordis to the ventricles (PQ) was kept variable and relatively small, and the time of conducting the stimulation along the ventricles (QRS complex) as a rule did not undergo any substantial variations, whereas the duration of the interval Q - T (time of the "electric systole") in the majority of subjects was clearly decreased. However, the decrease in the Q - T interval was expressed to a relatively smaller degree than the decrease in the R - R interval, with respect to which the value of the systolic characteristic, determined after Fogelson - Chernogorov, increased.

These changes in the EKG in te mountain climbers were expressed to a somewhat slighter degree than in the control group of subjects. The differences in the changes in the EKG up to an altitude of 7000 m were relatively small. At an altitude of 7000 m the dynamics of changes in the EKG differed substantially. In the mountain climbers the most clearly expressed hypoxic changes in the EKG were noted in the first 3 - 5 minutes, and then a partial normalization occurred. In the majority of these unconditioned subjects the hypoxic changes in the EKG for a period of a 5 - 10 minute residence remained sharply expressed and no tendency to normalization of the EKG was noted.

The dynamics of the changes in the bioelectric activity of the brain in the studies with the mountain climbers at altitudes of 5000-9000 m differed substantially from the dynamics of changes in the EKG in the control group. Thus, with the development of the acute hypoxic state in subjects of the control group the change to the left in the EEG was expressed to a significantly greater degree than in the mountain climbers. Here the distinct appearance of high-amplitude slow fluctuations in the process of "ascent" in the control group was noted somewhat earlier than in the mountain climbers. Thus at an altitude of 5000 m the distinct activation of the δ - and θ -rhythms was observed in 6 out of the 20 subjects of the control group and in 3 out of the 17 mountain climbers, and at an altitude of 6000 m in 9 out of 20 in the control group and in 5 out of the 17 mountain climbers.

At an altitude of 7000 m in all 20 of the control group a slow rhythm (2 - 7 Hz) was periodically distinctly expressed, and which disappeared only in three of the subjects after a 5 - 10 minute

residence at high altitude. In the mountain climbers during the first minutes of residence at 7000 m a periodic activation of the δ- and θ -rhythms was noted in 15 out of the 19 subjects, but after 5 - 10 minutes it was distinctly expressed only in two of them, whereas in teh others we observed a normalization of the EEG, /54 as a result of which the change to the side of dominance of the slow fluctuations almost completely disappeared.

It is known that between the appearances of hypoxic disorders in nervous activity and the change in the EEG-activation of slow rhythms there does exist a definite correlation [5-7]. The increase in hypoxic disorders of the central nervous system as a rule is accompanied by an increase in the number of θ- and δ -waves on the EEG.

In fact this correlation can be traced in the majority of subjects of the control group. Thus, in 16 of the subjects, simultaneously with the progressive increase in the EEG in the number and amplitude of the slow waves, we also noted a corresponding increase in the disruptions in the coordination of movements: characteristic disorders in writing, perseveration of letters, syllables and words and the appearance of errors in solving elementary arithmetical problems (addition, subtraction or multiplication of whole two-value numbers), an increase in the latent period of motive reactions, disorder in memory. Here only in three of the subjects who showed high tolerance to hypoxia was there not noted any substantial disorders in the meaningful content of the writing and even with the appearance of clonic spasms in the writing hand the subjects retained consciousness and noted motive disorders in themselves. In the mountain climbers no distinct correlation was noted between disruptions in the activity of the central nervous system and the corresponding changes in the EEG.

Of definite interest is the fact that during "ascents" to altitudes of 8000-9000 m and with brief residence there, in 8 of the mountain climbers there was no acceleration in the slow activity on the EEG. The development of an overall slow down and the appearance of clonic spasms in the writing hand were noted in them even on the background of desynchronization of the EEG with retention of consciousness.

We could judge the qualitative changes in the EEG from the change in total bioelectric activity. The significant increase in the total bioelectric activity with development of hypoxic hypoxia in all cases occurred due to the increase in the number and amplitude of slow oscillations. Here in the group of mountain climbers the total bioelectric activity with "ascent" to high altitude increased to a significantly smaller degree than in the control groups. Thus in the majority of subjects of the control group the total bioelectric activity even at an altitude of 7000 m increased by 4-5 times, whereas in the 11 mountain climbers it

increased only by 1.5-2 times, in 4 it remained without substantial changes and in 3 as a result of the expressed desynchronization it decreased by almost 2 times.

Analysis of the recordings of the state of being and the text which was memorized by rote showed that all the subjects, based on the character of the changes in text of the writing, may be /55
divided into three groups. In the first group belongs the majority of subjects, in whom at an altitude of 7000 m substantial disruption handwriting was noted as well as grammatical errors and errors in meaning. In the second group, crude errors were noted with relatively insignificant changes in the handwriting, for example, perseveration, omissions, etc. Finally in the third group who as a rule were highly tolerant of hypoxia, there were observed to a greater or smaller degree disruptions in handwriting but here the grammatical errors were missing and the meaningful content of the written material was retained. This group of subjects solved the arithmetical problems rather rapidly and correctly.

As already noted in mountain climbers to a significantly lesser degree there was expressed a change to the left on the EEG under conditions of hypoxic hypoxia. In this case it is obvious that in solving the arithmetical problems or during the time of recording the state of being the δ- and the θ -rhythms on the EEG as a rule to a significant degree were suppressed and a desynchronization was observed. It is significant that even when the suppression of rhythms was insignificant the meaning in the writing was found to be only slightly changes. Clear consciousness at high altitudes and the ability to retain a critical evaluation of condition and the surrounding environment is one of the characteristic peculiarities of the central nervous system in the mountain climber.

It is worth mentioning that in developing the hypoxic state at 8000-9000 m in many of the mountain climbers who were in a slow-down state (well expressed drowsiness, increase in related period of the motive and speech reactions) on the EEG instead of the usual increase in slow activity which is characteristic for unadapted subjects a desynchronization was observed.

Thus, on the basis of the research that was carried out we may conclude that persons who are repeatedly subjected for long periods of time to high altitudes from 2000-7500 m have an increased tolerance to acute hypoxia. There naturally arises the problem as to whether is this attained only in the process of acclimatization to high altitude conditions or does the occupation of mountain climbing in itself produce a certain selection as a result of which persons with high individual tolerance to oxygen deficiency are selected.

There is a basis to assume that acclimatization has significant value. We can judge about this on the basis of the dependence which we found of altitude tolerance on the number, and mainly the character of the ascents which were completed. Most tolerant of acute hypoxia were those persons who had previously completed ascents and attained altitudes on the order of 7000-7500 m. We can judge as to the leading role of acclimatization also from the responses of the mountain climbers themselves who note that during the time of the first ascents to altitudes of 4000-5000 m they /56
suffered from altitude sickness, in individual subjects this was rather severe.

As a result they either completely did not suffer altitude illness at these altitudes using the same schedule of ascent as previously or for a short period of time there appeared in them only slight symptoms of it, for example, a headache.

It is most essential to explain what characteristics of adaptation the mountain climbers possessed for such a high tolerance to acute hypoxia. Here at first it seems to be the hyperventilation which in mountain climbers during ascent in a pressure chamber was expressed considerably more sharply than in the control group. It should be noted that in its development the arbitrary increase in breathing is of definite significance. We can judge this based on evaluation of the state of being during the time of solving the arithmetical problems and in other instances when the attention of the subject was found to be distracted in carrying out any assignment, the pulmonary ventilation was decreased significantly and the saturation of arterial blood with oxygen was correspondingly decreased. The hyperventilation guaranteed substantial higher saturation of arterial blood in mountain climbers at altitudes of 5000-7000 m than in subjects of the control group.

Thus the high effectiveness of the function of internal breathing is one of the important characteristics of the reaction of mountain climbers to acute hypoxia.

Here we must nevertheless pay attention to the fact that the increase in breathing (increase in the minute volume of ventilation) is expressed differently not only in subjects of the control group but also in the mountain climbers.

In two of the mountain climbers out of 19 the hyperventilation at altitudes of 5000-9000 m was relatively low but in spite of this they showed high tolerance to acute hypoxia. These data permit us to assume that the physiological mechanism which determines the adaptation of an organism to oxygen deficiency in the inhaled air in different persons may be individually different.

One significant characteristic of the reaction of the central nervous system of subjects adapted to high altitudes to acute

hypoxia is the prolonged retention of consciousness and the ability for intellectual activity.

In no case did the crude disruptions of consciousness in the mountain climbers precede the appearance of the motive disruptions--the myospasm of the writing hand, whereas in subjects of the control group the spasms coincided in time with the appearance of the crude disruptions in consciousness or in several instances a disorder in consciousness was observed even earlier than the spasms. Here unlike subjects of the control group in the mountain climbers the change to the left on the EEG was lacking or was expressed relatively weakly.

This research showed that subjects who have been exposed repeatedly to high-altitude conditions and who have carried out prolonged heavy physical work possess a high tolerance to acute hypoxia. As the investigations of P.V. Vasil'yev, A.R. Kotovskaya, R.A. Vartvaronov, S.F. Simpur, G.D. Yukhnovskiy have showed these subjects as a rule also have a high tolerance to the effect of radial G-loads and to elevated temperature.

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THE EFFECT OF ADAPTATION TO HIGH ALTITUDE ON MAN'S TOLERANCE OF ACUTE HYPOXIA, HIGH TEMPERATURE AND VESTIBULAR IRRITATIONS

V.B. Malkin, G.D. Yukhnovskiy and S.S. Markaryan

ABSTRACT: In three different groups (mountain climbers, physically trained men and scientific staff) the tolerance of acute hypoxic hypoxia, high temperature and vestibular irritations was investigated before and after residence in mountains. The increase in tolerance to acute hypoxia in the majority of persons living for the first time under high-altitude conditions was established. The tolerance to elevated temperature after residence in the mountains was lowered insignificantly and the tolerance to vestibular irritations was somewhat increased.

An increase in tolerance of the effect of acute hypoxia in /57
healthy subjects after residence in mountains at altitudes on the order of 2000 - 7000 m has been noted by Sirotinin, Vladimirov, Malkin, Vasil'yev, Hartmann, Luft et al [2,4,5,7,8].

There exist data that daily training for a period of a month in a pressure chamber at an altitude of 6000 m of healthy subjects will lead to an increase not only of their altitude tolerance but also to the effect of high and low temperature [6].

The purpose of this research was to study the effect of adaptation to high-altitude conditions on the tolerance of healthy subjects to the effect of acute hypoxic hypoxia, high temperature of the environment and vestibular irritations.

The investigation was carried out with different groups of /58
healthy subjects: 11 highly qualified athlete-mountain climbers (1st group), 10 young, physically well-developed men (2nd group), who had previously not resided in mountains, and with 5 scientists (3rd group) who were participating in carrying out this research.

Adaptation to high altitude in five of the healthy subjects in 1964 was carried out gradually: 12 days at an altitude of 2000 m (Terskol); 12 days at an altitude of 3800 - 4200 m (Ledovaya) Baza and Priyut Odinnadtsati) and 5 days again at an altitude of 2000 m. In 1965 the time of residence at an altitude of 3800 and 4200 m was extended to 20 days for this same group of subjects.

The mountain climbers remained for a period of 6 days at an altitude of 2000 m (Terskol), after which they descended.

The group of scientists remained basically for a period of 25 - 28 days at an altitude of 2000 m (Terskol), but periodically (in connection with the research to be conducted) descended to Ledovaya Baza and for a brief time to Priyut Odinnadtsati. At Ledovaya Baza each scientist spent from 4 to 6 nights.

Before and after remaining in the mountains, a determination of the tolerance was made for each of the participants of the expedition. For this purpose, under pressure-chamber conditions, the subjects without oxygen in "stages" ascended to an altitude until distinct signs of a deep hypoxic state appeared, such as roughness in writing, losses in the ability to solve elementary arithmetical problems, cramps in the hand (writing cramps), different depth of disruption of consciousness.

In the first experiments with five subjects prior to and following ascent into the mountains, the altitude of the "ascent" in the pressure chamber did not exceed 7000 m and only the time of residence at this "altitude" was taken into account. In all the other studies the "ascent" was carried out according to the following schedule. To an altitude of 5000 m at a rate of 25 m per second and with a landing at each kilometer on the order of 15 - 20 sec; beginning from an altitude of 5000 m the landing at each subsequent altitude was five minutes.

In all of the subjects EEG's were taken on a multichannel ink-recording apparatus in the frontooccipital lead of an EKG in 3 standard leads and of respiration movement of the chest and periodically the blood pressure was taken. Simultaneously on an oximeter of "Krasnogvardeyets" type the saturation of the arterial blood with oxygen was recorded. Throughout the entire experiment a continuous observation was made on the behavior and overall condition of the subject.

To judge as to the ability to function and of intellectual activity the subjects, while remaining at high altitude, solved arithmetical problems (multiplication of two-digit numbers) and state of being was periodically recorded.

To study tolerance of the effect of high environmental temperature, 24 heat experiments were carried out in a thermal pressure chamber under conditions of normal barometric pressure at an environmental temperature of +70° C (the temperature of the chamber walls +90, +92° C) and a relative humidity of 40 - 65%. /59

The subject was placed in a chair in the chamber where there was no ventilation.

During the experiments the subject was continuously observed by a physician. Every 10 minutes successive physiological parameters were registered: EKG in the II lead; respiratory movement

of the chest; body temperature. At the end of the experiment water losses were determined.

Furthermore, the overall condition of the subjects were evaluated from their state of being and heat perception.

The EKG and the breathing were registered on an "Al'var" electroencephalograph. The body temperature was measured by an alcohol thermometer under the tongue. Water losses were determined by weighing the subjects before and after the experiment on medical scales.

In 10 of the subjects, before and after remaining at high altitudes, the functional condition of the vestibular analyzer was studies by continuous cumulation of coriolis accelerations). Using this method the subjects were rotated at a rate of 180° per second (1 turn in 2 seconds) in a special chair with the head and body in a vertical position and with eyes open. After 10 seconds following beginning of the rotation the subject in accordance with instructions inclined his head toward the right shoulder - this was the original position. From this position the subject turned his head toward the left shoulder every 5 - 6 seconds uniformly for 2 seconds then for the same period of time turned toward the right. The inclination of the head toward the shoulder was no less than 30° from the vertical on each side. The subject during the experiment reported on his state of being: on the appearance of the illusion of rocking and other sensations. With the occurrence of sickness, the time of its onset was registered which also determined the duration of the test.

From the discussion of experimental data we assume it to be feasible from the beginning to cite the results of the high-altitude investigations.

After remaining at high altitude, a distinct increase in the altitude tolerance was observed in five of the subjects who participated in the first expedition.

Four of the subjects, after remaining at high altitude, were able to stay at an altitude of 7000 m without oxygen for a period of 20 - 30 minutes, retaining fully a satisfactory overall condition and a sufficiently high level of ability to function. Prior to the high-altitude trip these subjects could remain at this altitude only for 1 to 8 minutes.

In later investigations we were able to change somewhat the method of determining altitude tolerances in connection with which /60 we attempted to compare the data from experiments carried out with different groups of subjects.

As our previously conducted research showed (see this collection, Russian page 147, English page 164*. Mountain climbers have

* Translator's note: not translated.

a high background altitude tolerance and as a rule during a relatively long time feel well at an altitude of 7000 m. Therefore in working with this group of subjects, it was necessary to make ascents to high altitudes.

TABLE 1. CHANGES IN THE ALTITUDES TOLERANCE PRIOR TO AND AFTER RESIDENCE AT HIGH ALTITUDES.

Subject	Prior to Mountains		After Mountains for 4-6 days		After Mountains for 28-31 days		Tolerance
	Altitude, m	time min. & sec.	Altitude, m	time min. & sec.	Altitude, m	time min. & sec.	
			Group 2				
A-v	9	2,00	8	5,00	8	5,00	Lowered
V-vo	8	3,10	9	1,00	8	5,00	Increased
K-as	7	5,00	8	4,30	8	3,40	"
Sh-k	8	1,30	9	1,10			"
Ku-s	9	0,50	9	2,20	9	1,40	"
			Group 1				
Ts-n	8	4,00	8	4,00			Unchanged
K-v	9	1,50	8	5,00			Lowered
B-n	9	1,10	9	3,20			Increased
K-yev	9	1,50	9	2,10			Unchanged
T-m	8	2,00	9	2,45			Increased
S-t	9	2,40	9	2,20			Unchanged
B-ov	9	0,40	9	2,00			Increased
N-v	8	1,30	8	5,00			"
G-r	8	5,00	9	1,40			"
B-d	9	0.40	9	2,10			"
M-r	9	1,10	9	1,10			Unchanged
U-a	8	1,20	8	4,30			Increased
R-a	7	1,10	8	2,30			"
L-a	7	1,30	8	2,00			"
M-ko	6	5,00	7	1,50			"
M-ns	5	4,30	5	5,00			Unchanged

Table 1 gives data on the altitude tolerance for 3 different groups of subjects prior to and after residence under high-altitude conditions.

For the young subjects who went into the mountains for the first time and who felt well at high altitudes and completed a successful ascent to the eastern peak of Elbrus, their time spent in the mountains led a pronounced (in 3 out of 5) increase in altitude tolerance. For one of the subjects who suffered from altitude sickness, the tolerance was somewhat lowered and for one who had a high background tolerance it was increased very little. /61

The change in altitude tolerance in mountain climbers was very insignificant. For four it varied practically none at all (improvement of less than 30 seconds), for one it was lowered and for six it was increased. However in 2 of the 6, the increase was caused by the fact that the background tolerance in them was lowered due to fatigue.

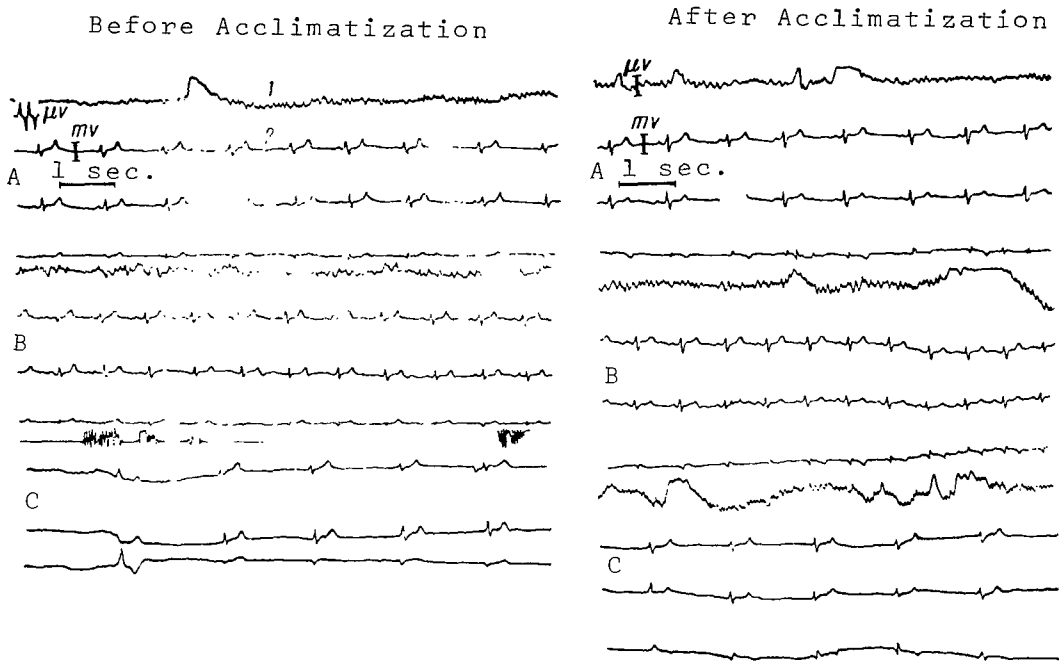
Any substantial increase in the tolerance of this group was in fact only in three subjects, two of which entered the mountains after a relatively prolonged interval. This apparently produced in these persons a lower background tolerance.

We attempted to find the dependence between the adaptation process in mountains and the high tolerance of the mountain climbers. For two of the mountain climbers (Ts-n and K-v) who had the greatest load and who had lived at altitudes on the order of 4000 - 4800 m for a longer time than the others, no increase was noted in their altitude tolerance; for one it was lowered, in the other it remained without substantial changes.

To explain these results of excessive physical load is premature, since for the mountain climbers, including Ts-n and K-v after expeditions to Tyan'-Shan (Khan-Tengri Province) with a large load (complex ascent with relatively prolonged residence at altitudes of 6000 - 7000 m) a slight increase was noted in their altitude tolerance.

For three of the scientists out of five after remaining at high altitudes, a distinct increase was found in their altitude tolerance, for one it was increased insignificantly and for another, who had low tolerance it remained without change. This last case (M-is) deserves special attention since even before the trip into the mountains, in the pressure chamber at an altitude of 5000 m after 4 minutes, 30 seconds, he lost consciousness with unexpectedly developed bradycardia, that was accompanied by convulsions. At high altitudes M-is functioned at altitudes of 3800 - 4200 m and felt fully satisfactorily, however after reaching an altitude of 5000 m in the 5th minute again his cardiac contractions slowed down, and the precollaptoidal condition occurred again (see the figure).

First of all we are interested in the causes that, after adaptation at high altitudes, lead sometimes to a sharp increase in altitude tolerance. Analysis of the data of registration of the physiological parameteters showed that in those persons there was noted at high altitude a sharp increase in breathing, as a result of which during the ascent to high altitude after remaining in the mountains the saturation of arterial blood with oxygen was considerably higher than in the control ascent.



EKG and EEG of Subject M-s during Ascent to an Altitude of 5000 m. 1. EEG left frontal-occipital lead; 2. first; 3. second; 4. third standard EKG lead. A. Before ascent; B. 5000 m, 1 min; C. 5000 m, 4 min. 30 sec. /62

This latter probably determined the improvements from the side/63 of the higher nerve activity and the bioelectric activity of the brain. After returning from the mountains they retained their ability to function with relatively little change in the EEG for a more prolonged time than before residence in the mountains.

It is worth noting that the saturation of arterial blood with oxygen at the moment that the high-altitude test ceased in persons who have shown an increase in tolerance was the same as in the control study or, in individual cases, even somewhat higher. This indicates that residence in mountains (adaptation to chronic hypox-

ia) gives no possibility to an organism to retain a sufficiently high level of ability to function under conditions of lower oxygen supply, but it is accompanied by a more effective and normal activity of the functional systems, which determine the transport of oxygen to the tissue structure which are more sensitive to hypoxia.

The unexpected improvements in altitude resistance in the various groups of subjects probably to a certain degree are due to differences in the duration of the process of acclimatization itself.

It is of interest to note the fact that altitude tolerance, just as tolerance to the effect of transverse G-loads, after high-altitude adaptation is partially retained for a period of a month and even longer time. The results of the heat experiments were unexpected for us. We assumed that residence in high altitudes would lead to an increase in tolerance of the subjects to high temperature. Moreover, in the experiments on animals carried out in conjunction with F.V. Babchinskiy, slight increase was noted in the survival of mice adapted at high altitudes at a temperature of +60° C. A similar effect was described by F.T. Agarkov [1] earlier.

The data which we found show that after 10 - 14 days following return from high altitudes in the majority of subjects a slight decrease is observed in their tolerance to high temperature. Here it is quite important that for almost all of the subjects following residence at high altitudes the increase in body temperature - the basic sign characterizing the reaction of an organism to overheating - occurs more rapidly than in the control experiments.

After return from high altitudes the overall condition of the subjects at the end of their stay in a heat chamber was considerably worse than in the control experiments. This is explained by the fact that in two of the subjects after adaptation at high altitudes at the end of the experiment a precollaptoidal condition set in, whereas all the control experiments ceased on request of the subjects due to the appearnace in them of unpleasant heat sensations. Thus, the impression was created that, in spite of the ability of the subjects after adaptation to high altitude to withstand more pronounced increases in body temperature, their tolerance was nevertheless found to be somewhat lowered.

The results of the investigation on tolerance of subjects to vestibular irritations are shown in Table 2. As is obvious from these data, prior to acclimatization in five subjects the time of endurance of cumulation of Coriolos accelerations was within a range of 2.5 to 6 minutes, and they belonged to the group of vestibular - tolerant subjects, the other five subjects - to vestibular tolerance since the tolerance time varied from 18 - 100 seconds. /64

Under the influence of high altitude acclimatization in the majority of subjects (in 7 out of 10) a prolongation was observed

TABLE 2. DETERMINATION OF VESTIBULAR TOLERANCE BASED ON THE METHOD OF ACCUMULATION OF CUMULATION OF CORIOLIS ACCERLERATIONS.

Subject	Tolerance time, min., sec.		Difference	Subject	Tolerance time, min., sec.		Difference
	Before Acclimatization	After Acclimatization			Before Acclimatization	After Acclimatization	
K-v	3.45	9.05	+5.20	U-n	0.18	0.45	+0.27
V-ko	4.30	12.00	+7.30	S-t	1.10	1.35	+0.25
Ku-s	2.30	3.30	+1.00	G-r	1.40	2.20	+0.40
K-as	6.00	6.00	0.00	N-v	1.05	1.30	+0.25
A-v	4.00	1.00	-3.00	K-ov	1.25	1.00	-0.25

of the tolerance time to Coriolis accelerations. This was noted especially in the 3 vestibular - tolerant subjects in whom tolerance was increased by 1 - 7.5 minutes. In four of the vestibular tolerant subjects the changes were quite insignificant, the time increased by 20 - 40 seconds and in one of the subjects from this group a decrease in the tolerance time was noted. From the group of vestibular - tolerant subjects, no change was noted in one of them and in one of them, A-v, who suffered altitude sickness, the vestibular tolerance was lowered significantly.

Analysis of the experimental data indicates that acclimatization in mountains as a rule promotes an increase in tolerance to the vestibular analyzer. This probably is associated with the fact that under conditions of hypoxia the sensitivity of the vestibular analyzer first increases and then gradually decreases.

CONCLUSIONS

1. After adaptation to high-altitude conditions at altitudes of 2000 - 4000 m an increase in altitude tolerance is noted in healthy subjects who had previously not resided at such altitudes. The sharpest high-altitude tolerance increases in subjects who have been actively and sufficiently long acclimatized at altitudes on the order of 3800 - 4200 m.

For the majority of mountain climbers after active acclimati- /65
zation at such altitudes no substantial increase was noted in their altitude tolerance.

2. After adaptation to high-altitude conditions a slight decrease was noted in tolerance to high environmental temperature, whereas the body temperature in the subjects in the heat chamber was increased more rapidly than in the investigations carried out prior

to high-altitude exposure.

3. After exposure at high altitudes, in seven of the 10 subjects, an increase in tolerance to vestibular irritations was noted.

4. In the subject who had suffered altitude sickness after exposure at altitudes of 2000 - 4200 m a decrease in altitude and vestibular tolerance was noted.

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EFFECT OF REPEATED RESIDENCE IN MOUNTAINS ON THE TOLERANCE OF MOUNTAIN CLIMBERS TO ACUTE HYPOXIA

N.M. Asyamolova and V.B. Malkin

ABSTRACT: This research was conducted with 12 mountain climbers who were master athletes. Before and after the high-altitude expedition in the region of Tyan'-Shan' (maximum altitude 6995 m) their altitude tolerance was determined under conditions of gradual ascent in a pressure chamber and their blood was examined.

It was established that a visit of 5 - 6 weeks by the mountain climbers who had previously participated numerous times in high-altitude ascents, produces a relatively insignificant increase in their tolerance to acute hypoxia. No correlation was established between the increase in altitude ceiling and changes in the blood: increase in the number of erythrocytes and the hemoglobin.

Earlier we showed that the tolerance of mountain climbers to acute oxygen starvation is considerably higher than in those unadapted to high-altitude conditions (control group). The idea naturally arises that residence at high altitudes each time produces certain adaptation changes in the organism which can be summarized. In this respect it is of definite interest to study the altitude tolerance of mountain climbers before and after repeated residence at high altitudes. In the literature available to us we were unable to find any special research devoted to this problem. The authors who studied the increase in tolerance of healthy subjects after residence at high altitudes in the majority of cases made their observations on members of the scientific expeditions, i.e., on persons as a rule who had previously not been specially acclimatized to high-altitude conditions [1-6]. One exception only is the investigation of Hartmann et al. [7] who worked with a group of young men (8 subjects), who had been occupied for a rather long period of time with mountain climbing. Let us note that in these research projects, after residence in mountains following different periods of time subsequent to decent from high altitudes, there was noted a differently expressed increase in the altitude tolerance. According to the data of Hartmann et al. after prolonged residence in the Himalayas (4 months) including a period of several weeks at altitudes on the order of 6000-7000 m the altitude tolerance in 7 out of 8 subjects was increased. This increase was established after 1.5-2 months following return from the mountains but it was relatively small.

/66

Here it is significant that it was not possible to detect a strict correlation between the duration of residence of the subjects at high altitude and the respective increase in tolerance to acute oxygen starvation. This latter probably is due to the extremely prolonged residence of the expedition at high altitudes.

The basic task of the present paper was to study the effect of repeated residence under high-altitude conditions on the tolerance of mountain climbers to acute hypoxic hypoxia. With this purpose in mind, after 18-23 days following return from the mountains in 12 of the mountain climbers we made a determination of their altitude tolerance under conditions of gradual "ascent" in a pressure chamber. We can judge the conditions of acclimatization at high altitudes from the fact that it was carried out in the region of Tyan'Shan' where 5 subjects made an ascent to the top of Khan-Tengri (6995 m) but the basic group, who did not participate directly in reaching the peak, remained for a long period of time at altitudes of 4000-6000 m, periodically carrying out heavy physical work.

The methods of the investigation, directed at the establishment of an "altitude ceiling", i.e., the boundaries of the individual altitude tolerance, have already been described in a previous report and we shall not pay any special attention to them here. To set forth this research it is feasible to begin from the data which characterized the altitude tolerance before and after residence at high altitude. We can judge the changes in the altitude tolerance in 12 mountain climbers after 3 weeks following the high-altitude expedition based on data which are presented in Table 1 where the properties which characterize altitude and time of residence there are given for all subjects before and after residence at high al- /67
titudes.

As is obvious from the Table, in 9 of the subjects following residence in the mountains, a small increase was noted in the "altitude ceiling", and in 3, these facts are of definite interest; therefore let us look briefly at the characteristics of these subjects. In the mountain climber D-n the Adams-Stokes syndrome appeared. During his ascent in the pressure chamber to an altitude of 7000 m, a progressive decrease appeared in the pulse rate on the EKG after 25 sec. A rapid descent from high altitude then followed. In the process of descent, the heart activity suddenly ceased in the subject. The heart stoppage continued for 18 seconds and was accompanied by loss of consciousness and a spastic seizure in the form of an epileptic spasm. After 3-4 sec following disappearance of the pulse, sharp changes appeared in the bioelectric activity of the brain. After a short phase of hypersynchronization, an almost complete inhibition of the biopotential of the brain (Fig. 1) appeared. On the figure are shown the recordings of the EKG, EEG and breathing movements, taken at an altitude of 7000 m.

We can distinctly see the gradually increasing slow heart activity, the cessation of the heart with the simultaneous appearance of high amplitude flow oscillations on the EEG and finally the de-

TABLE 1. TIME (In Min and Sec) OF RESIDENCE OF MOUNTAIN CLIMBERS AT VARIOUS ALTITUDES DURING "ASCENT" IN A PRESSURE CHAMBER BEFORE AND AFTER HIGH ALTITUDE ASCENT.

Subject	7000 m		8000 m		9000 m		10,000 m	
	Before	After	Before	After	Before	After	Before	After
S-t	-	-	-	-	1.00	5.00	-	-
B-dt	-	-	-	-	2.00	5.00	-	-
Ts-in	-	-	-	-	1.10	5.00	-	-
T-m	-	-	-	-	1.30	3.00	-	-
B-yev	-	-	-	-	2.00	5.00	-	-
B-ov	-	-	-	-	2.30	-	-	1.30
M-yn	-	-	-	-	1.20	3.00	-	-
B-in	-	-	-	-	2.00	5.00	-	-
L-ov	25.00	30.00	-	-	-	-	-	-
K-ov	-	-	3.00	5.00	-	-	-	-
Ts-ov	4.00	3.00	-	-	-	-	-	-
D-n	0.40	-		-	-	-	-	-

velopment of biopotentials of the brain: on the EKG are seen the /68
first heart contractions. The beginning of the pulse rate was on the order of 30 beats/min and then gradually increased and after 30 sec reached 54 beats/min. After 1.5-2 minutes, the consciousness and the active condition was restored in the subject but still for a period of several minutes we noticed a certain weakness and slow-down. Thus in this case we may speak essentially about a man with grave functional disorders in the nervous regulation of the cardiac activity. It is interesting that this subject, who was a master athlete, during the period of residence at high altitudes up to 6200 m, retained a sufficiently good state of being and was able to /69
carry out heavy physical labor with which he managed (in the opinion of the other members of the expedition) even better than the others. With repeated ascent in a pressure chamber it seems maximal caution was exercised and, in particular, continuous registrations of the EKG were carried out due to which (unlike the first test) at the very beginning of development of bradycardia the subject was given oxygen which prevented the development of deep disruptions in cardiac activity (Fig. 2). It is significant that at this moment when a slight sharpening in the frequency of the heart contractions was noted in him, the subject indicated a deterioration in his state (nausea occurred). The second subject Ts-ov was a mountain climber /70
of the first category and also a highly qualified athlete.
The distinguishing mark of his body structure was the good development of his skeletal musculature. In this subject during the first

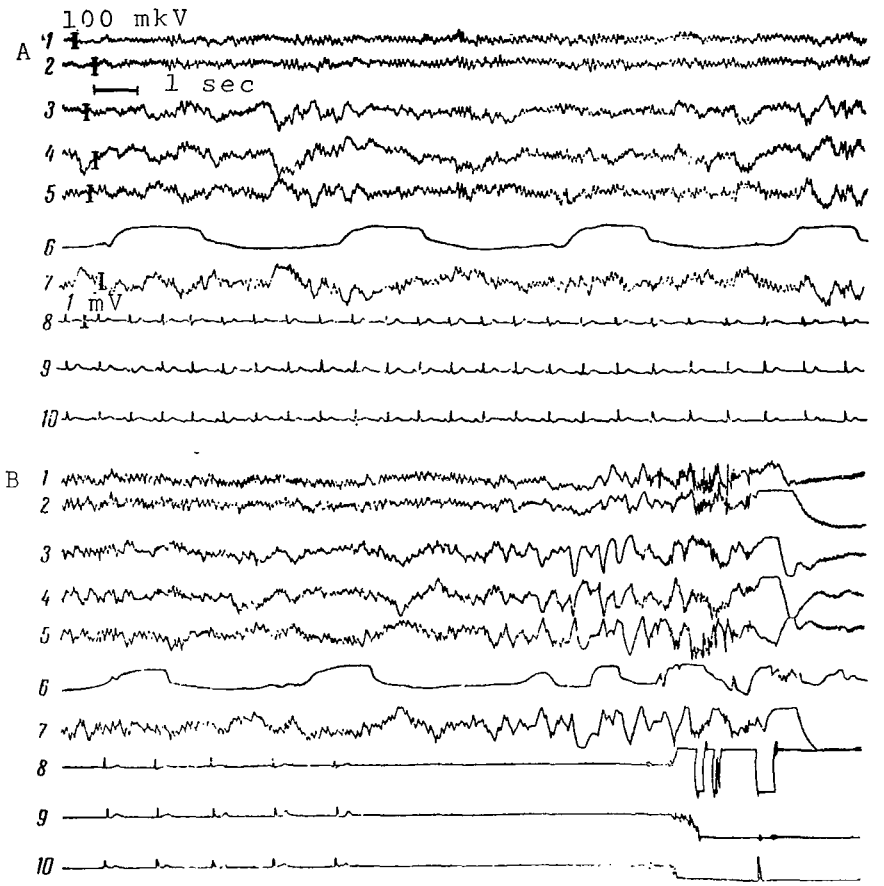

Fig. 1. EEG and EKG of the Subject D-n Before Residence at High Altitude. EEG: 1. Left Frontal Occipital; 2. Right Frontal Occipital; 3. Left Frontal Monoplar; 4. Right Frontal Monopolar; 5. Left Occipital; 6. Respiration; EKG: 8, 9, 10, I, II and III Standard Leads: A. Altitude 7000 m, 1-3 Minutes; B. 7000 m, 5th Minute.

ascent (prior to the expedition) an "altitude ceiling" of 7000 m was established where for 4 minutes there was observed in him a sharp slowdown chronic spasms of the muscles of the writing hand and a significant decrease in the level of consciousness. In this respect we made the recommendation to pay especially careful attention to the adaptation of Ts-ov to high altitude since it was found to be lower than in the other subjects. However in connection with the conditions constructed, Ts-ov was found to be in the front group and along with his companions reached the peak of Khan-Tengri. Here he felt so unsatisfactory that he could not descend from the peak alone. After 3 weeks following completion of the high-altitude expedition there was determined an altitude tolerance in the pressure

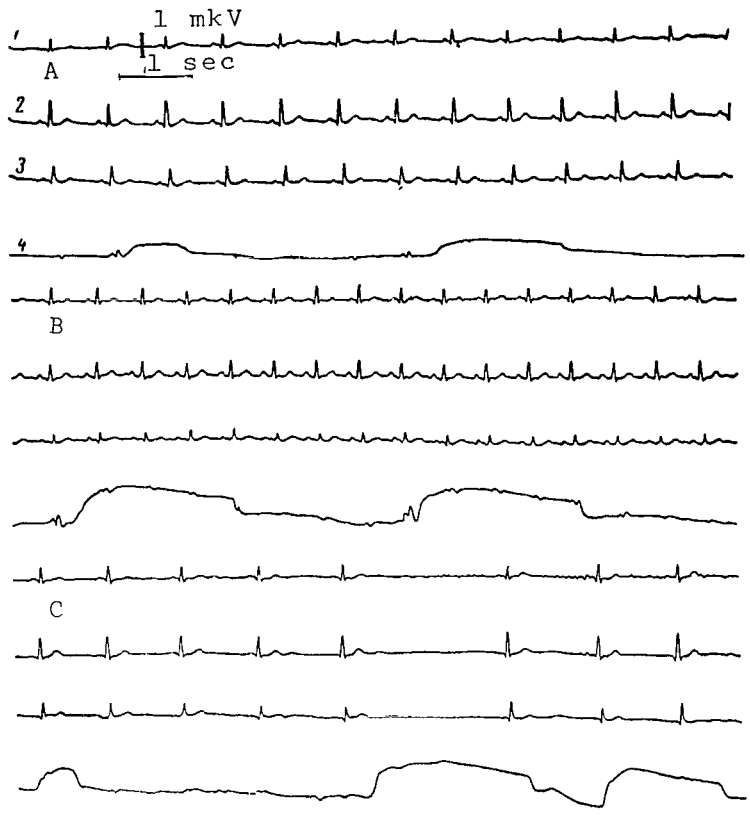

Fig. 2. EKG of the Subject D-n During Ascent to an Altitude of 6000 m Following Residence at High Altitudes. A. Before Ascent; B. 5000, m, 5-th Minute; C. 6000 m, 5th Minute. 1, 2, 3. I, II and III Standard EKG Leads; 4. Respiration.

chamber for Ts-ov. In the background recordings on the EKG there periodically appeared ventricular extrasystoles which in the first test had not appeared. At altitudes of 6000-7000 m the extrasystole was increased and there was noted a large localization of centers. At an altitude of 7000 m the subject remained approximately 1 minute less than before the ascent. The hypoxic state (symptomocomplex, characterizing development of deep disorders of the central nervous system) was the same as in the investigations carried out prior to the expedition.

In 9 of the subjects, as is obvious from Table 1, there was observed an insignificant increase in the "altitude ceiling". But they all noted that residence in the pressure chamber the second time adapted them easier than the first time and this difference was especially well expressed at altitudes of 6000-7000 m. We could even note slight divergences between the data of determining the "altitude ceiling" from the physiological characteristics and the

subjective evaluations of the results of the pressure-chamber investigations carried out before and after the expeditions.

It was interesting to compare several characteristics which characterize the functional state of the systems of the blood, respiration, blood circulation and the central nervous system with a given "altitude ceiling" before and after the expedition. These differences were found on the whole to be insignificant. One exception involved the data from the hemotological investigation (Table 2).

Although in 7 of the subjects there was established a slight increase in the "altitude ceiling", however no regular increase in the hemoglobin and erythrocytes was noted. Moreover it is of definite interest to look at the subjects (master athlete S-t and B-ov) in whom, after the expedition, both the hemoglobin and the number of erythrocytes were significantly decreased. At the same time they showed a higher tolerance to acute hypoxia. Thus in the mountain /71
climbers there was no correlation detected between the number of erythrocytes, the hemoglobin and the altitude tolerance. In comparing the data which characterize the functional stress of the internal breathing no substantial differences were observed in frequency, depth, amount of ventilation and saturation of arterial blood with oxygen before and after the high-altitude expedition.

TABLE 2. NUMBER OF ERYTHROCYTES IN THE HEMOGLOBIN OF MOUNTAIN CLIMBERS AFTER 21 DAYS FOLLOWING DESCENT FROM THE MOUNTAINS.

Subject	Hemoglobin, %	Erythrocytes, 1000	Subject	Hemoglobin, %	Erythrocytes, 1000
S-t	16,6 / 13,3	4410 / 3650	K-ov	14,0 / 16,0	4500 / 5050
M-in	16,6 / 17,7	4800 / 4850	B-in	13,3 / 17,3	4350 / 5050
T-m	14,6 / 14,3	6100 / 6500	B-v	15,0 / 10,3	4300 / 3300
B-ov	15,3 / 15,3	4400 / 4200			

Comment. The numerator is before residence in the mountains; the denominator is after residence.

It was also impossible to detect any substantial difference in the changes of frequency in the heart contractions on the EKG. Data from electroencephalographic investigations were also quite similar and only in individual subjects was there noted during the ascent in the pressure chamber after the expedition a somewhat more slightly expressed change in the biopotentials to the left, (the appearance of slow oscillations). Comparison of the recordings of the state

of being permitted us to make the conclusion that the change in handwriting with the second ascent was somewhat less expressed than in the first investigation. However, as noted previously, the subjects themselves noted that their state of being became somewhat better.

On the basis of analyzing the obtained data we may come to the conclusion that, in subjects who have been exposed repeatedly to high-altitude conditions and who already possess a high tolerance to hypoxia, residence in the mountains for a period of 5-6 weeks at altitudes up to 6000-7000 m produces only an insignificant increase in the "altitude ceiling". This gives a basis for assuming that a substantial increase in the altitude tolerance of mountain climbers occurs apparently as a result of the first 3-4 times in the mountains after which the increase in tolerance is no longer significant.

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TOLERANCE OF ANIMALS TO HYPEROXIA, HYPERCAPNIA AND HIGH TEMPERATURE AFTER ADAPTATION TO LOWERED BAROMETRIC PRESSURE.

F. V. Babchinskiy, V. B. Malkin and G. D. Yukhnovskiy

ABSTRACT: This research was conducted on white mice. The tolerance of the animals was studied according to their survival in conditions of a gaseous atmosphere containing 96% oxygen with an elevated amount of CO_2 (40%) and high temperature (50-60%) before and after adaptation to conditions of lowered barometric pressure.

It was established that adaptation to hypoxia will not result in an increase in the tolerance of animals to the effect of hyperoxia and high CO_2 concentration in the inhaled air. The tolerance to high temperature in the adapted animals increases slightly.

/72

In studying the process of adaptation hypoxia many investigators have paid basic attention to the effects which indicate a nonspecific increase in the tolerance of the adapted animals to different adverse influences [1,2].

By developing this point of view several authors [1,2] assumed that adaptation to hypoxia in essence must be accompanied by an increase in the tolerance of the adapted animals to practically any adverse environmental factor.

At the same time analysis of changes which occur with the development of adaptation to hypoxia shows that the majority of reactions which determine the restructuring of the organism have a rather specific character. They are directed toward an increase in the oxygen transport to the tissues and to the cellular structures of the brain which are especially sensitive to oxygen deficiency. Thus the works of P. Ber, I. M. Sechnov, D. Barcroft, Holden, Hurtado and others [3, 4, 8, 9, 12] established that an increase in the minute volume of pulmonary ventilation, the oxygen capacity of the blood and an increase in the blood flow through the lungs, heart and brain is one of the important adaptation reactions with hypoxic hypoxia.

/73

In this respect there arises the question as to whether the adaptation to hypoxic hypoxia can be accompanied by less in the tolerance of animals to the effect of certain adverse environmental factors, the adaptation to which produces a restructuring of the organism in its character that is opposite to that observed

with hypoxia. To study this problem we made an investigation of the tolerance of animals adapted to hypoxia to such influences as increased oxygen content in the inhaled air (95%), increased amount of carbon dioxide (up to 40%) and high temperature of the environment (+60°C).

The adaptation reactions which arise with oxygen deficiency are opposite those which occur under the effect of an oxygen excess.

We can judge this on the basis that an increased amount of oxygen in the inhaled air in man and animals produces a decrease in the ventilation of the lungs [7, 11], a decrease in the number of heart contractions (6, 10), a drop in the amount of hemoglobin and the number of erythrocytes in the peripheral blood. These reactions are opposite those which occur with hypoxia and are directed to guarding the organism from an increased amount of oxygen. Hence it is of interest to study the changes in the tolerance of an organism to acute hypoxia after a prolonged effect of hyperoxia.

On the other hand A. G. Zhironkin [5] established the possibility of increasing the tolerance of animals to the toxic effect of high oxygen pressures by preliminary conditioning them to oxygen deficiency. As one of the probably mechanisms of adaptation the author assumes that the hyperoxia of tissues on this basis is "hyperoxic hypoxia" and the effect of hypoxic conditioning is specific and directed to the adaptation to different forms of hypoxia including the "hyperoxic".

Consequently, it is necessary to explain if the adaptation of the organism to hyperoxia occurs in general and if the change in tolerance to hyperoxia occurs following prolonged high-altitude and pressure-chamber adaptation.

With adaptation to hypoxic hypoxia there is developed a hyperventilation as a result of which the tissues which undergo oxygen deficiency are simultaneously located in a state of hypocapnia. Here there is a basis for assuming that the tolerance of animals to high concentrations of CO_2 in the inhaled air may be lowered.

In the process of adaptation to hypoxia an essential role is played by the restructuring of the blood circulation, in particular the redistribution of the blood stream, increase in the blood stream through the brain, lungs and heart and a respective decrease in the blood stream through the skin, muscles and internal organs. With an increase in temperature of the atmosphere the adaptative reactions of the blood circulation have to a significant degree an /74
opposite character.

In our experiments we set the purpose of explaining the change in the tolerance of an organism to the following adverse factors:

To hyperoxia after high-altitude and pressure-chamber adaptation;

To an increased concentration of carbon dioxide in a gaseous atmosphere;

To elevated temperatures;

To acute hypoxia after prolonged effect of hyperoxia.

The investigations were carried out on white mice. Experiments with hyperoxia were set up in a chamber especially prepared of organic glass which guaranteed visual observation of the animals with retention of a constant gaseous atmosphere.

Ventilation of the chamber with pure oxygen or with a mixture with nitrogen was carried out from high-pressure tanks. Through the reductors with a course and fine regulation, the gases were admitted through the hose with a calibrated rheometer and then to the gas mixer and into the chamber.

Humidity and carbon dioxide were removed from the chamber by ventilation. Furthermore, during the day a small pump was turned on which circulated the "air" of the chamber through chemical absorbents of carbon dioxide and moisture.

Feed, bedding and other objects were placed into the chamber through a receiver-transmitter hatch which was hermetically sealed. All manipulations in the chamber were carried out using rubber gloves with long hands that were attached to the projection of the openings on the sides of the walls. Removals from the chamber were made every day. The gas composition of the chamber was controlled on an Ors and "Khelige" gas analyzer.

Adaptation of the animals was carried out in mountains at altitudes of 2000 m (Terskol) for a period of 16 days and at an altitude of 3800 m (Ledovaya Baza) for 14 days. Interrupted adaptation in the pressure chamber was accomplished by daily ascents for a period of 13 days to ever-increasing altitudes up to 7000 m.

In the first series of experiments we determined the lifetime of the mice at an "altitude" of 9000 m following introduction of 90-92% oxygen for a period of 2, 3 and 4 days.

The experimental results showed that the tolerance of the animals to acute oxygen starvation is decreased, this being to a larger degree as the duration of priming with oxygen is increased. The difference in the altitude tolerance of the control mice and the experimental mice is especially pronounced during the first minutes of the effect of hypoxia. In proportion to their residence at high altitudes this difference was gradually smoothed out (Fig. 1).

The basic reason for lowering the tolerance of an organism to acute hypoxia is apparently disruption in the gaseous metabolism produced by damage to the lungs which develops under the effect of hyperoxia. In this respect we set up one more experiment on determing tolerance to acute oxygen starvation following the effect of /75 lower (subtoxic) concentrations of oxygen.

The mice (11 in number) were kept for 2.5 days in a gaseous environment consisting of 40 and 60% oxygen with a mixture of nitrogen. Then along with the control animals they were subjected to ascent in a pressure chamber to altitudes of 9000 and 10,000 m Exposure at each altitude was 10 minutes.

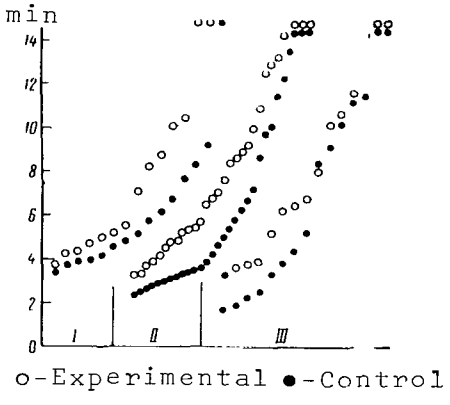

Fig. 1. Lifetime of the Mice at an "Altitude" of 9000 m Following Two (I), Three (II) and Four (III) Days of Residence in an Atmosphere of Pure Oxygen.

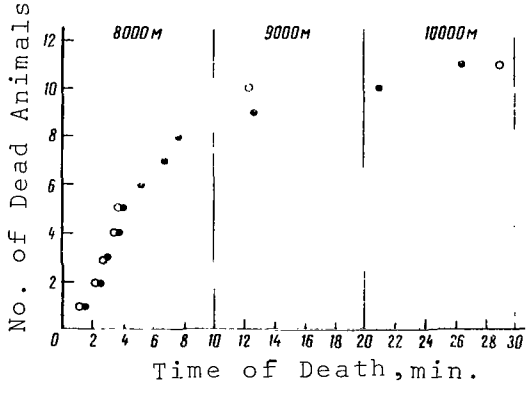

Fig. 2. Changes in the Tolerance of Mice to Acute Hypoxia After Residence in a Hyperoxic Gaseous Medium.

The average lifetime at "high altitude" of the mice who have previously been exposed to a hyperoxic gaseous medium was 8 min 30 sec and the control animals was 6 min., 36 sec. (Fig. 2).

By comparing the results of these two experiments we can come to the conclusion that the toxic concentrations of oxygen decrease /76 but the nontoxic probably increase slightly the tolerance of animals to acute hypoxia.

The second series of experiments was carried out to determine

the survival of animals in an atmosphere of pure oxygen after high altitude and interrupted pressure-chamber adaptation.

The results of the first two experiments of this series showed that in a hyperoxic atmosphere the animals who were acclimatized at "Ledovyaya Baza" died somewhat earlier than those from "Terskol". However, on the 5-6th days of priming this difference disappeared and all the animals died almost simultaneously (Table 1).

TABLE 1. SURVIVAL OF MICE IN AN ATMOSPHERE OF PURE OXYGEN ON THE THIRD (I) AND NINTH (II) DAYS FOLLOWING HIGH-ALTITUDE ADAPTATION

Group *	on 4th day	on 5th day	on 6th day	Group *	on 4th day	on 5th day	on 6th day
I				II			
"Ledovaya"	2	5	3	"Ledovaya"	2	4	4
"Terskol"	3	4	3	"Terskol"	-	5	5
Control	1	5	4	Control	-	3	7

*Each group has 10 animals.

Under analogous conditions we carried out two experiments on mice following interrupted pressure-chamber adaptation. No substantial statistically meaningful distinctions in change of tole rance of the animals to hyperoxia appeared here.

Thus the adaptation reactions which arise with adaptation of the organism to oxygen deficiency not only do not protect but to some degree even facilitate in several of the animals an earlier development of the pathological process which is produced by the toxic effect of pure oxygen.

In the third series of experiments we determined the tolerance of mice to high concentrations of carbon dioxide in a mixture with oxygen following pressure-chamber and high-altitude adaptation.

The first experiment was set up on 10 mice on the second day after cessation of the interrupted pressure-chamber adaptation (carried out in the period from the 8th to the 22nd of December, 1964) and on 10 control animals. In the chamber we created a stream of a gaseous mixture, 1.2 liters/min in volume enriched with CO_2.

The average lifetime of the mice in this gaseous atmosphere was: The adapted animals 171 min (a range from 43 to 282 min) and the control animals 156 min (from 69- 282 min).

The second experiment was carried out on 15 mice on the 8th day following a month high-altitude adaptation and on 15 control animals. The stream of the gaseous mixture was created the same but the carbon dioxide content in the first three hours was increased from 27 to 43% after which it remained constant. /77

The average lifetime of the mice "acclimatized" in mountains was 300 minutes (from 208 to 373 min) and the control animals 296 minutes (from 210 to 363).

In spite of the fact that the overall lifetime of the mice in the first and second experiments was different (in connection with a nonidentical percentage content of carbon dioxide in the gaseous atmosphere of the chamber), the time of death of the experimental and the control mice was practically the same. In the fourth series of experiments we determined the effect of pressure-chamber and high-altitude adaptation on the tolerance of animals to elevated temperature.

The first 2 experiments were carried out at a temperature of the surrounding atmosphere of 60° C every 1-2 days following a single and a three-time interrupted adaptation of the mice in the pressure chamber.

In these experiments the mice who were adapted to high altitudes (especially following a three-time repetition of adaptation) were found to be more tolerant of high temperatures than were the control animals (Table 2).

TABLE 2. THE EFFECT OF INTERRUPTED PRESSURE-CHAMBER ADAPTATION ON THE SURVIVAL OF MICE AT A TEMPERATURE OF 60°

Group	No. of Animals	Time of Death, Min.				
		10	20	30	40	50
After first adaptation	20	2	9	6	3	-
After third adaptation	20	-	6	9	3	2
Control	20	5	14	1	-	-

The third experiment was set up at a temperature of 50 ± 2° after 5-8 days following a month's adaptation of mice at high altitudes (Fig. 3). In these less strict temperature conditions the average lifetime of the mice adapted to high altitude was 58 minutes, 2 seconds, and the control animals was 31 minutes, 43 seconds, i.e., a high tolerance to elevated temperature was observed in the animals adapted to hypoxia.

By estimating the results of all the series of experiments it follows first of all to note that adaptation to hypoxia does not

lead to an increase in the tolerance of animals to the effect of hypoxia and a high concentration of CO_2 in the inhaled air.

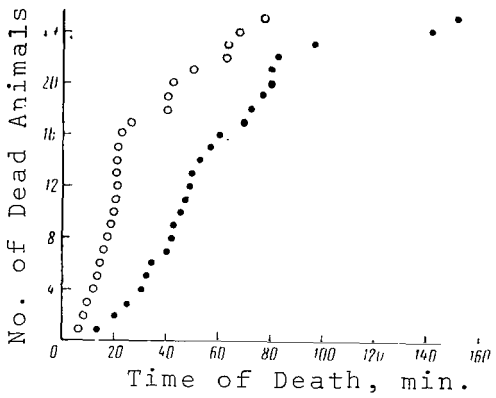

Fig. 3. Survival of Mice at a Temperature of 50 ± 2° C. Designations are the Same As in Figure 1.

If the criterion of tolerance is assumed to be the survival of the animals under changed conditions, then it is correct to assume that the practically identical lifetime of the control animals and those adapted to hypoxia in a gaseous environment, enriched with oxygen and carbon dioxide indicates a slight decrease in the tolerance of the adapted animals to these factors. Such a conclusion is based on the fact that the agonic phase during the time of which there appeared acute hypoxia is found to be more lengthy in the adapted animals. As a result of this the time of survival in the control animals and the experimental animals is practically the same, however, the time of retention of a relatively high functional level under these influences in the experimental animals as a rule is somewhat shorter than in the intact animals. Thus the results of the work indicates that a nonspecific increase in the tolerance of the animals who were adapted to hypoxia to noxious factors does not appear in all cases. It is missing when the damaging effect leads to the development of adaptational specific reactions having an opposite direction to the adaptive reactions developing during hypoxia. /78

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EFFECT OF ADAPTATION TO LOWERED BAROMETRIC PRESSURE ON TOLERANCE OF HYPOCAPNIA

A.K. Kochetov

ABSTRACT: Twenty-four subjects participated in the research, of which 12 were mountain climbers. The hypocapnic state was induced at normal barometric pressure by the method of voluntary hyperventilation. The EEG's, EKG's blood pressure and pCO_2 in alveolar air were recorded.

It was shown that mountain climbers are more tolerant of hypocapnia than those subjects who have not been conditioned to high altitude. Thus, in subjects of the control group, the average increase in frequency of heart contractions was 12% greater than in the mountain climbers. Stronger changes were observed on the EEG in comparison with mountain climbers in spite of the fact that in these latter the pCO_2 in alveolar air was reduced to lower values. No substantial difference was found in the reactions of the blood pressure.

These investigations showed that in the process of adaptation to high-altitude conditions the human organism reaches a higher tolerance of hypocapnia.

In the research conducted by Sirotinin, Vladimirov, Asyamolovaya and Malkin, as well as others, it was noted that the tolerance to hypoxic hypoxia in subjects adapted to high altitude is considerably higher than in unconditioned subjects [1, 3, 4].

Investigations of a group of mountain climbers showed that in the majority of them the increase in altitude tolerance was due basically to the considerable increase in pulmonary ventilation. In this respect, during the time that the mountain climbers remained at altitudes of 5000 - 7000 meters, they underwent a high saturation of arterial blood with oxygen and a lower partial pressure of CO_2 in the alveolar air as compared to the subjects of the control group.

There naturally arises the idea that during the period that they remain in the mountains in the process of conditioning man to oxygen starvation there is simultaneously developed an adaptation to hypocapnia which always accompanies hypoxic hypoxia. Here we may assume that in such subjects the increased tolerance to hypo-

capnia appears even under conditions of normal oxygen supply.

To explain this question we carried out investigations with 12 mountain climbers - master athletes age 26-40, who systematically /80 participated in high-altitude expeditions. As the control group we chose subjects who has passed the medical commission and who were permitted to make high-altitude ascents but who were not especially conditioned for a prolonged period of time under conditions of a rarefied atmosphere.

For creation of hypocapnia we used an arbitrary measured hyperventilation. For control of the amount of ventilation the subjects wore on their chests a rubber jacket which was filled with air. The rubber jacket was connected to a special pneumatic instrument of Moreyer capsule type, the recorder of which during inspiration and expiration was deflected to a strictly determined value as a function of the respirational volume. On the drum of the kymograph the paper was traced in such a way that the subject could follow the path of the pen and keep the frequency and depth of respiration established by the experimenter. The frequency of breathing was 30 per minute, the respirational volume was 2000-2200 cm^3, the volume of pulmonary ventilation 60-66 l per minute. The subjects were hyperventilated up to the appearance in them of the first "unusual" or even "unfavorable" sensations which were expressed in the form of paresthesia of different characteristics, vertigo, nausea or visual disorders. At the moment that such sensations appeared and then during the period of the distinct appearance on the EEG of slow oscillations, the intake of alveolar air with a subsequent determination in it of CO_2 (Holden apparatus) was measured.

Registration of the physiological functions was carried out on a 12-channel EEG from the firm "Saney". The recording from the EEG was accomplished bipolarly from the frontooccipital regions and monopolarly from the region of the sinciput, the temple, the occiput, both with open and with closed eyes. The EKG was simultaneously recorded in three standard leads; in several of the experiments the blood pressure was determined.

The data characterizing change in pCO_2 of the alveolar air, the pulse rate and the complaints of the subjects during the time of hyperventilation are shown in Table 1. As is obvious from the average time of hyperventilation prior to the appearance of unfavorable sensations in the group of mountain climbers was more prolonged (2 minutes, 20 seconds) than in subjects of the control group (1 minute, 40 seconds). In this case the average value of the alveolar pCO_2 for which the sensations in the mountain climbers occurred was 42.6 mm Hg, in the control group it was 24.5 mm Hg. The mean value in the increase of pulse rate during the time of hyperventilation in the control group was more significant (66%) than in the mountain climbers (54%) in spite of the higher degree of hypocapnia which was expressed in them.

In subjects of both groups in the process of hyperventilation the sensations occurred after different intervals of time and different values of the alveolar pCO_2. Thus in several of the mountain climbers the sensations appeared with a decrease in the alveolar pCO_2 to significant values (18.2, 19.2 mm Hg), whereas other /81
complaints appeared with a relatively high pCO_2 (26-27 mm Hg).

In the majority of mountain climbers the sensations appeared in the form of different types of paresthesia. The subjects of the control group in the majority of the investigations noted the beginning of vertigo or visual disorder and only at the end of hyperventilation did complaints appear of paresthesia.

To establish the physiological improvement which determined the characteristics of the course of the hypocapnic syndrome in the mountain climbers we attempted to compare the changes in the EKG and the EEG of the mountain climbers and in subjects of the control group.

As we know, the most constant symptom of hyperventilation is tachycardia. In our experiments during hyperventilation an increase in pulse rate was noted in all subjects. In this case no strict dependence was found between the degree of increase in pulse rate, changes in the EKG and the level of decrease in pCO_2 in alveolar air. Thus in three of the subjects with a relatively small degree of hypocapnia, 24-27 mm Hg, the pulse rate increased to 88-180% of the original values, whereas in others with a decrease in alveolar pCO_2 to 18-20 mm Hg, the pulse was increased only to 41-58%. In spite of this difference in the appearance of individual reactions, from the side of the cardiovascular system, to hypocapnia the average increase in frequency of cardiac contractions in the subjects of the control group was 12% greater than in the mountain climbers.

The overall direction of changes in the EKG in the subjects of both groups was characterized along with the sinusal tachycardia, increase in the wave voltage R_1 and T and an insignificant increase in the wave R_3. The time of the heart cycle decreased basically due to the decrease in the interval T-P, i.e., as a result of shortening the period of diastola in connection with which the value of the systolic characteristic determined according to Fogelson-Chernogorov increased.

The degree of decrease in the T waves as a rule depended on the original value; with higher T waves there was noted a more expressed flattening.

The described changes in the EKG during the time of hyperventilation were observed in the majority of subjects of the control group (9 subjects). In the group of mountain climbers these changes in the EKG were noted only in four experiments. In one of the mountain climbers the decrease in the waves P_1 and P_2, T_1

TABLE 1. ALVEOLAR pCO_2, PULSE RATE AND COMPLAINTS DURING MEASURED HYPERVENTILATION

No.	No. pCO_2, mm Hg		Time of Hyperventilation Before Onset of Adverse Sensations		Pulse at Moment of Onset of Adverse Sensations						Character of Sensations	
					Mountain Climbers			Control				
	Mountain Climbers	Control	Mountain-Climbers	Control,	Background	At Moment of Sensation	Increase,	Background	At Moment of Sensation	Increase,	Mountain Climbers	[illegible]
1	39,2—23,2	41,0—27,0	2'10"	1'14"	60	90	50	66	108	63	Heat	Vertigo
2	41,2—18,2	41,0—24,0	3'30"	1'45"	72	102	41	66	102	54	Paresthesis	Same
3	37,4—20,3	38,6—27,1	2'20"	50"	66	100	51	78	114	46	Vertigo	»
4	39,9—23,2	40,1—25,0	1'50"	2'00"	72	108	50	66	108	63	Paresthesis	Paresthesis
5	37,2—24,6	36,2—[illegible]	1'50"	2'20"	66	108	63	66	100	51	»	»
6	38,6—26,0	38,[illegible]	1'25"	1'30"	66	114	72	72	114	58	»	»
7	39,2—20,3	[illegible]	1'46"	1'15"	78	126	61	66	132	100	»	Vertigo
8	37,2—24,7	38,0—23,2	2'00"	2'10"	66	90	36	72	136	89	»	The Same
9	41,3—26,6	38,1—22,2	58"	2'35"	54	102	88	54	84	55	Light Vertigo and Paresthesis	Vertigo Heat
10	38,9—22,5	40,0—24,3	2'40"	2'30"	66	98	48	72	150	108	Paresthesis	Vertigo
11	40,1—19,2	38,2—32,3	3'40"	1'03"	72	114	58	78	108	38	Feeling of Inebriation	The Same
12	39,0—22,6	39,7—27,6	2'10"	48"	66	90	36	60	104	73	Paresthesis, Vertigo	Heat, Paresthesis
M	22,6	24,5	2'10"	1'40"			54			66		

and T_2 were associated with the phase of respiration. In inspiration the wave voltage decreased. In one case, hyperventilation produced a disruption in cardiac rhythm which was expressed in the appearance of individual ventricular extrasystoles.

In studying the recordings of blood pressure during the time of hyperventilation we were able to find certain dynamics in its change. Thus at the beginning of hyperventilation the blood pressure, both systolic and diastolic was decreased; then in proportion to the development of hypocapnia as a rule there appeared a diastolic pressure. The systolic pressure in one of the subjects increased insignificantly, reaching the original value, in others it remained, as before, at a slightly decreased level. No substantial difference in change in blood pressure during the time of hyperventilation between the mountain climbers and the subjects of the control group was noted.

Changes in the EEG during the time of hyperventilation have /83
been described by many authors who have widely used hyperventilation as functional test for the appearance of latent forms of epilepsy [2, 5, 6]. In the literature which is available to us we have found no indications where the authors, in describing the EEG during the time of hyperventilation, have taken the characteristics of the background EEG into account.

In subjects with a flat EEG (up to 20 mkv) the hyperventilation either produced an insignificant increase in amplitude of the biopotentials without visible changes in its frequency or was completely unaccompanied by changes in the bioelectric activity.

In the development of hyperventilation syndrome no strict dependence was established between the subjective sensations and the character of change in the bioelectric activity of the brain. At the moment that the sensations appeared in the subjects there was noted on the EEG different changes: the activation of α or β rhythm, the appearance of short groups of slow oscillations of increased amplitude. At the same time in several of the subjects even before the appearance of sensations on the EEG there was clearly observed the activation of δ and θ rhythms.

In comparing changes in the EEG at the time of hyperventilation in mountain climbers and subjects of the control group it was found that in the majority of mountain climbers (in 8) on the EEG at the moment of the appearance of unusual sensations there was noted an insignificant activation of the α rhythm or an increase in the high-frequency rhythms. In subjects of the control group the hyperventilation produced stronger changes in the EEG which were characterized by the appearance, in the majority of cases at the moment of the sensation, of individual or diffuse slow oscillations.

Thus the increased tolerance to hypocapnia in the majority of

mountain climbers on the ground in comparison with subjects of the control group indicates that in the process of adaptation to conditions of high altitude the human organism reaches an increased /84 tolerance of hypocapnia. It was quite extraordinary that the increased tolerance of hypocapnia appears not only the lowered barometric pressure under the conditions of oxygen deficiency but is also retained for a prolonged period of time after descent from the mountains. At the same time, in spite of the altitude conditioning, individual differences in the tolerance of hypocapnia are nevertheless retained. Certain subjects, probably those who are highly sensitive to CO_2 loss, in spite of the lengthy time which they spent at high altitudes do not substantially increase their tolerance of hypocapnia. On the basis of this research we can state as a working hypothesis the position that periodic conditioning to hypocapnia on the ground may increase the tolerance of man to the effect of hypoxic hypoxia.

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THE TOLERANCE OF ANIMALS TO ACUTE HYPOXIA AFTER CONDITIONING TO PHYSICAL LOADS UNDER HIGH-ALTITUDE CONDITIONS

Ye.V. Loginova

ABSTRACT: This research has been conducted on white mice and rats. The mice were conditioned to both static (hanging on poles) and dynamic (running on a treadmill) work, the rats only to dynamic. The conditioning was carried out under middle-altitude conditions (altitude of 2000 m). The changes in weight of the animals, number of erythrocytes, the amount of hemoglobin, the oxygen requirements and the lifetime at altitudes of 9000 - 12,000 m were determined. It was found that conditioning to dynamic work under middle-altitude conditions slightly increases the tolerance of rats of acute hypoxia: such conditioning to static loads under these same conditions does not affect the tolerance of the organism to acute hypoxia.

The question as to the mutual influence of conditioning to physical loads and adaptation to high-altitude conditions has great practical significance and is of definite theoretical interest. The practical significance of the question is concerned, on the one hand, with the fact that for physiologists of sport it is important to explain the influence on athletic accomplishments of the repeated use of physical exercises under conditions of a slight oxygen deficiency in the inhaled air; on the other hand, for aviation and space medicine, it it necessary to solve the problem of /85 including physical loads in the schedule of adaptation to hypoxic hypoxia.

Conditioning to muscular activity, in the opinion of the majority of investigators, in itself causes an increase in the tolerance to different adverse factors including acute hypoxia [3,4,11,12]. N.V. Zimkin, M.M. Bogorad, L.P. Zimnitskaya and others feel that the nonspecific effect on an organism of physical exercise has no less importance than does the specific effect of one or another factor [9].

Without denying the fact that, with an increase in tolerance to one of the irritants, the reaction of the organism is changed to some degree to the effect of the others, M.Ye. Marshak and his associates emphasize the great significance of the principle of "nonspecificity" in the development of the process of adaptation [15,17].

The physiological mechanisms of conditioning to physical loads to some degree is similar to the restructuring of the organism in the process of adaptation to hypoxia. With intense muscular activity, just as with hypoxic hypoxia, there is developed in man a hypoxemia due to the noncorrespondence between the transport and the requirements of oxygen [13,14,16]. In this respect we can expect positive results from the cumulation of changes produced by conditioning to physical loads and adaptation to hypoxia. However, it should be borne in mind that along with the overall changes in the functional state with physical conditioning and adaptation to hypoxia there are also substantial differences produced in first order by important factors such as CO_2. One characteristic of the adaptation to hypoxemia during motive activity is the simultaneous adaptation to hypercapnia, whereas with adaptation to hypoxic hypoxia an adaptation to hypocapnia is developed. Therefore, the adaptation mechanisms in both cases may have substantial differences.

Experimental work on the problem of the mutual influence of muscular conditioning and adaptation to hypoxia may be divided into three groups.

The first group of investigations carried out with athletes was devoted to the influence of preliminary adaptation to hypoxia under high-altitude conditions on the subsequent activity of these or other physical exercises. A.P. Frolov, D.A. Alipox and others note a positive character of such an influence on the increase in athletic accomplishments [2,22].

The second group contains those investigations which were carried out mainly on animals in which a positive effect was shown of conditioning to muscular exercises on the tolerance to acute hypoxia [5,6,10,23].

In the third group of investigations, data are cited on the cumulation of changes during physical conditioning under hypoxic conditions [20,25]. P.K. Stoyanov studied changes in the EKG, blood pressure and vital capacity of the lungs in humans, both those who were involved with physical labor at high altitude and /86
those who were not. The data obtained indicate that there is a difference in the functional changes in these two groups of subjects: in those who were engaged in physical labor the author observed a significant increase in the pulse rate, the arterial pressure, and an insignificant decrease in the vital capacity of the lungs at the beginning of residence at an altitude of 2925 m. In proportion to the adaptation, changes in the blood pressure gradually returned to the original level - the pulse became slightly more frequent even and the vital capacity of the lungs was greater than the original values. In persons who were not involved in physical labor, from the moment of arrival at high altitude and for the period of the entire six months of observation the pulse rate and the arterial pressure had a tendency to increase, and the

vital capacity to decrease.

In the work of Clark et al there is some indication that in rats conditioned on a treadmill under hypoxic conditions the myoglobin increased by 50% in comparison with the animals who were conditioned under ordinary conditions [25].

By analyzing the literature data we come to the conclusion that apparently there is developed a certain cumulation of changes associated with conditioning to physical loads and adaptation of the organism to hypoxia. The nature of this phenomenon is quite complicated and its rules have been studied insufficiently. We can only assume that the cumulation includes changes which occur at various levels of regulation of the organism.

The present work is a part of the investigations whose purpose is to explain, on the one hand, the most optimal conditions for summation of the changes which occur as a result of the physical conditioning and adaptation to hypoxia and, on the other hand, to attempt a study of the mechanisms which form the basis of this summation.

In this report we give results of investigations in which we compare the influence of conditioning to static and dynamic loads under high-altitude conditions on the adaptation effect determined basically from the tolerance of animals to acute hypoxia.

The work was carried out on 180 white mice and 45 white rats. The mice were divided into 6 groups, with thirty in each:

Group 1: Control, Moscow;

Group 2: Mice, subjected for 33 days to high-altitude conditions at an altitude of 2000 m above sea level;

Group 3: Mice, conditioned to static loads at an altidude of 2000 m;

Group 4: Mice, conditioned to dynamic work at an altitude of 2000 m;

Group 5: Animals subjected to an altitude of 2000 m for 14 days and to an altitude of 3800 m for 19 days;

Group 6: Mice, conditioned to static loads at altitudes of 2000 and 3800 m.

The rats were divided into three groups: /87

Group 1: Control;

Group 2: Animals subjected for 33 days to an altitude of

2000 m.

Group 3: Rats conditioned to dynamic work at an altitude of 2000 m.

Conditioning to static and dynamic loads wes carried out every other day, beginning from the 6 - 8th day of residence at high altitudes. For conditioning of the mice to static loads we used vertical poles. The animals were constrained on them for the first two days without load. From the third day a load of 10 g was suspended from the tail of the animal (the weight of the mouse was from 16 - 18 g). The load was gradually increased as the time the animal remained on the pole was increased. The first three tests of the mouse was for 5 minutes. From the fourth test this time was extended by 1.5 minutes with each test. In all 13 conditioning periods were made.

To condition the mice and rats to dynamic work we constructed a special treadmill. The rate at which the animals ran was maintained constant: 24 m per minute for the mice and 36 m for the rats. The conditioning to dynamic loads for the rats was begun with a path of 120 m. This load was maximal for the rats. We included in our problem carrying out conditioning to loads of average intensity, therefore from the third test the length of the path was decreased to 36 m. The conditioning of the mice was begun from 24 m.

The load for the rats was increased with each conditioning test by increasing the length of the path by 6 m (14 tests in all). In the mice such an increase in load occurred only in the first four tests after which until the end the load remained constant (13 conditioning tests).

In all groups of animals regularly during their residence under high-altitude conditions and upon return to Moscow we studied the changes in the amount of hemoglobin, the number of erythrocytes, the reticulocytes and eosinophils (the blood was taken from an incision at the end of the tail), we studied the oxygen requirement after Kolabukhov. In the conditioned animals the oxygen requirement was determined both before and after the load for the 5th - 15th minute of the recovery period every minute, then every 20 - 30 minutes, 40 - 50 minutes, 60 - 70 minutes and after three hours. Upon return to Moscow in all three groups of animals we determined the lifetime under conditions of ascent in a pressure chamber. The mice were raised at a rate of 75 - 80 m/sec to altitudes of 9000 m. At this altitude the first 10-minute rest was taken. Another 10-minute rest was given after each 1000 m. The rats were raised to 11,000 m. The first rest was for 10 minutes, then each 5 minutes every 1000 m. The condition of the animals and the dynamics of their death were fixed as a function of the "altitude" and time of residence.

Residence of the rats at an altitude of 2000 m led to a slight /88
increase in the erythrocytes and did not change the amount of hemoglobin.

Changes in the red blood in the mice differed from the changes in the rats. In the mice the number of erythrocytes increased gradually. In comparison with the group of animals who remained in Moscow, their increase was 15%. The amount of hemoglobin for the entire extent of residence in the mountains varied in a wave shape: during the first eight days there was observed a drop in the hemoglobin on the average from 15 to 11 g%; by the 18-24th day the amount of hemoglobin increased to 18 g% and then again decreased insignificantly by the end of the expedition.

The first days of residence in the mountains were accompanied by a significant drop in the number of eosinophils both in the mice and in the rats by an increase in the number of reticulocytes. From the 8 - 10th day the number of eosinophils in the peripheral blood began to increase gradually and by the end of residence exceeded the original values by approximately 3 times. The number of reticulocytes on the contrary decreased slightly (Table 1).

TABLE 1. CHANGES IN THE NUMBER OF RETICULOCYTES AND EOSINOPHILS IN RATS AND MICE IN THE PROCESS OF ADAPTATION TO HYPOXIA AT AN ALTITUDE OF 2000 m (AVERAGE VALUES).

Animals	n	Number of eosinophils per 1 cm³							Number of reticulocytes by 1000				
		Before Adaptation	During Adaptation, days				After Adaptation, days			Before Adaptation	During Adaptation, days			After Adaptation
			3–4	9	18–19	33	3	11	20		3–4	9	18–19	
Rats	8	98	17	—	95	349	110	—	—	22	190	—	88	14
Mice	10—15	102	22	61	—	288	81	85	65	—	—	44	32	30

The effect of dynamic loads and conditioning to them produced changes in the red blood in the rats and the mice.

In the rats, after carrying out the first two tests, there was observed a decrease in the number of erythrocytes by 25%, on the background of increase in hemoglobin by 25% in comparison with the unconditioned animals. By the end of the cycle in both groups of animals the number of erythrocytes and the amount of hemoglobin were equal (Fig. 1).

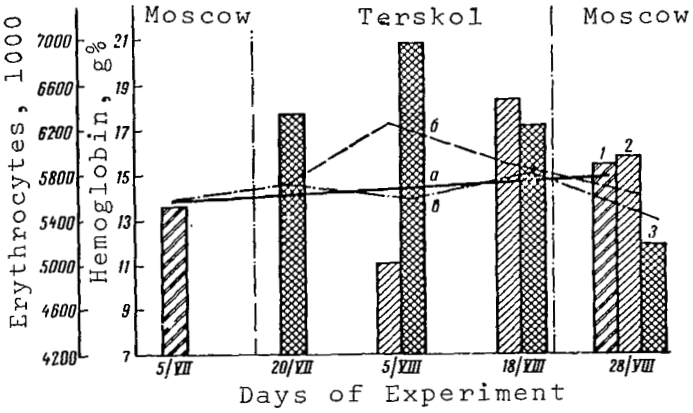

Fig. 1. Effect of Conditioning to Dynamic Work Under Middle-Altitude Conditions on the Number of Erythrocytes and the Amount of Hemoglobin in Rats. Erythrocytes: 1. Control; 2. In Animals with Dynamic Load; 3. Intact. Hemoglobin: a. Control; b. In Animals with Dynamic Load; c. Intact.

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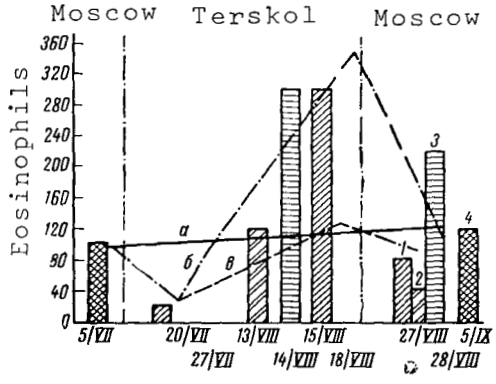

Fig. 2. Effect of Conditioning to Dynamic and Static Loads under Medium-Altitude Conditions on the Amount of Eosinophils in the Peripheral Blood. Mice: 1. Intact; 2. With Dynamic Load; 3. With Static Load; 4. Control. Rats: a. Control; b. Intact; c. With Dynamic Load.

In the mice the conditioning to dynamic loads produced the same increase in the number of erythrocytes as in the passively adapted animals. In the conditioned mice the amount of hemoglobin gradually and insignificantly decreased. As shown above, in the passively adapted animals no drop in hemoglobin was observed, and its changes had an expressed wave-shape character. /90

Both in the mice and in the rats conditioned to dynamic load, unlike those who were only adapted, no eosinophilia was noted - the number of eosinophils did not exceed the values which are characteristic for Moscow (Fig. 2). This effect is worthy of attention. The eosinophilia observed under high-altitude conditions was assumed by several of the investigators to be a symptom which indicates a functional exhaustion of the adrenal glands. The lack of eosinophilia in animals who underwent conditioning to dynamic work under high-altitude conditions contradicts this point of view. The reaction of the reticulocytes in conditioned mice and rats did not differ from the reaction in the unadapted animals.

The decrease in the number of erythrocytes in rats expressed at the beginning of conditioning was associated apparently with deepening of the hypoxic state under the influence of extreme muscular load (the first two tests with maximal load). We may assume that the accumulation in the blood of incompletely oxidized products of decomposition leads to an acceleration of destruction of the erythrocytes. A further increase in the number of erythrocytes indicates a correct choice of the intensity of conditioning schedule and its positive influence on the organism. Our data agree with the results obtained by G.A. Goryanaya [8].

Change in the weight of the conditioned and unconditioned rats at an altitude of 2000 m confirms this assumption. The weight of both groups varied approximately the same. Here the weight of the animals adapted to mountainous conditions, lagged from the weight of the control group who remained in Moscow (the weight of the adapted animals was 243 g, those passively adapted to hypoxia was 235 and the control animals was 260 g).

Only the mice were adapted to static loads. This conditioning was not manifested in the changes in the studied blood characteristics. The amount of hemoglobin, number of erythrocytes and eosinophils in the conditioned mice was the same as in the unconditioned animals.

Thus the reaction of the red blood and the eosinophils to conditioning to dynamic work differed from the reaction to conditioning to static loads.

Residence at high altitude led to a slight increase in the oxygen requirements of the animals in comparison with the control group. In the mountains, for the animals who were adapted to dynamic work, there was the greatest oxygen requirement. Upon

return to Moscow the oxygen requirement of this group of animals was the least. The group of animals conditioned to static loads did not differ in oxygen requirements from the group of unconditioned animals.

These data indicate that conditioning of animals to dynamic work under high altitude conditions was reflected by the degree, /91 and in several instances also by the character, of the physiological changes which occur in the process of conditioning. Conditioning to static loads was not accompanied by any peculiar characteristics.

As was shown above, after return to Moscow for all groups of animals, we investigated the tolerance to acute hypoxia.

Residence at an altitude of 2000 m without conditioning not only did not give an increase in tolerance to acute hypoxia but also produced even a slight statistically unreliable decrease.

The rats who were adapted to dynamic work under high-altitude conditions increased their tolerance to acute hypoxia (Table 2).

TABLE 2. LIFETIME OF DIFFERENT GROUPS OF RATS UNDER CONDITIONS OF ACUTE HYPOXIA (11,000 - 13,000 m)

Group	After Completion of Adaptation			
	Third day		12th day	
	Lifetime, min	P	Lifetime, min	P
Control, Moscow	11.3	< 0.5	7.8	> 0.5
Adaptated, 2000 m	9.7	> 0.01	5	< 0.5
Conditioned at 2000 m	15.8	< 0.5	9	> 0.5
Control, Moscow	11.3		7.8	

In the mice on the third day following completion of the conditioning and adaptation we did not observe any higher tolerance in comparison to the passively conditioned animals. The differences in the altitude tolerance between the animals subjected to an altitude of 3800 m (Ledovaya Baza) and the mice subjected at this altitude to conditioning to static loads, were statistically unreliable. The effect on tolerance to acute hypoxia of adaptation at different altitudes is clearly shown in Table 3.

On the 28th day the mice who were conditioned to dynamic loads, unlike the other groups of animals, still retained an increased tolerance to acute hypoxia ($P > 0.01$).

The lack of any influence from conditioning to static loads on the tolerance to acute hypoxia is associated apparently with

the fact that in itself the static loads do not produce any increase in the hypoxic state: saturation of blood with oxygen, as a rule, in carrying out static loads, does not change or changes incomparably to a lesser degree than with dynamic work [5-7]. Omission of the hypoxemic factor which is basic and common for the oxygen deficiency and the physical loads, probably is explained by the absence of a "nonspecific" influence of conditioning to static loads on the tolerance to acute hypoxia. /92

TABLE 3. LIFETIME OF MICE AT AN ALTITUDE OF 9000 - 12,000 m (AVERAGE VALUES FOR 9 - 10 ANIMALS).

Group	After Completion of Adaptation			
	4th day		28th day	
	Lifetime	P	Lifetime	P
3800 m, unconditioned	24 min 35 sec	< 0.5	2 min 53 sec	< 0.5
3800 m, "static"	28 " 20 "	> 0.1	2 " 31 "	< 0.5
2000 m, unconditioned	16 " 42 "	< 0.5	2 " 02 "	< 0.5
2000 m, "static"	11 " 07 "	< 0.5	1 " 42 "	> 0.01
2000 m, "dynamic"	11 " 44 "	> 0.01	6 " 47 "	> 0.01
Intact, Moscow	3 " 28 "		1 " 45 "	

Thus, conditioning to dynamic work under high-altitude conditions somewhat increases the tolerance of the rats to acute hypoxia; conditioning to static loads in the schedule which we chose under high-altitude conditions does not influence the tolerance of the organism to acute hypoxia.

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MUTUAL EFFECTS OF CONDITIONING TO PHYSICAL LOADS AND ADAPTATION TO HYPOXIC HYPOXIA

Ye.V. Loginova

ABSTRACT: This research was conducted on white rats. The animals were conditioned in running on a treadmill under ordinary atmospheric conditions under middle-altitude conditions (altitude of 2000 m) and under atmospheric conditions with parallel interrupted adaptation of the rats to hypoxia under pressure-chamber conditions (altitude of 3000 - 7000 m). We studied the change in weight of the animals, the number of erythrocytes, amount of hemoglobin and life time of the animals under conditions of acute hypoxia.

It was established that the isolated effect of only one conditioning to physical loads and even the parallel effect of conditioning to physical loads and adaptation to hypoxia did not lead to an increase in the tolerance of acute hypoxia. An increase was observed only with conditioning under middle-altitude conditions.

The question concerning the mutual effect of conditioning to physical loads and adaptation to hypoxia in spite of the multitude of research remains debatable (see in the present collection the article by Ye.V. Loginovaya, "Tolerance of Animals to Acute Hypoxia After Conditioning to Physical Loads Under High-Altitude Conditions").

In the first report data are cited which indicate the possibility of cumulation of changes associated with the physical load and a moderate degree of hypoxia with their simultaneous effects. /94

In this paper we have changed somewhat the conditions of the experiment. Conditioning to physical loads was carried out, not with an oxygen deficiency, but under ordinary laboratory conditions in which case these animals were adapted to hypoxia and in parallel under pressure-chamber conditions.

The experiment was carried out on 44 white rats who were divided into 4 groups:

Group 1: 12 rats subjected to interrupted pressure-chamber adaptation and parallely to conditioning to dynamic loads on a

treadmill;

Group 2: 12 animals who were conditioned only to dynamic loads;

Group 3: this group consisted of 10 rats adapted to hypoxia under pressure-chamber conditions;

Group 4: a control group kept under the conditions of the vivarium in Moscow.

Interrupted adaptation to hypoxia in a pressure chamber was carried out for a period of 13 days with a constant increase in "altitude" from 3000 to 7000 m. The daily time spent by the animals at this "altitude" was 6 hours $\pm$ 20 minutes. During this time the chamber was continuously ventilated so that the CO_2 did not exceed 1%, the humidity 60-80% and the temperature 23-25° C. We carried out this interrupted adaptation since it is highly effective and permits us to carry out a parallel conditioning to physical loads.

Conditioning to physical loads was carried out each day in a special treadmill. The rate of running of the animals was maintained constant 36 m/min. The load was increased with each conditioning cycle because of the increase in the path by 6 m. Altogether 14 conditioning exercises were carried out. This conditioning schedule was proven by us in the expedition to Mount Elbrus where it gave positive results.

Regularly in all of the animals before, during and after the conditioning cycle, we determined the weight, amount of hemoglobin, number of crythrocytes, reticulocytes and eosinophils in the peripheral blood. The blood was taken from a cut at the end of the tail.

After ending the conditioning in all groups of animals we determined the lifetime under conditions of gradual "ascent" in a pressure chamber. The rats "ascended" at a rate of 75-80 m/sec to the "altitude" at which they died. The first ten minutes "rest" was at 11,000 m, then 5-minute rests were repeated every 1000 m.

Adaptation of the animals to hypoxia was accompanied by an increase in the number of erythrocytes in the hemoglobin and a lag in the weight of the rat (Table 1).

Conditioning of the animals to dynamic loads produced a slight increase in the number of erythrocytes and a statistically valid increase in the hemoglobin in comparison with unconditioned animals./95

The increase in the number of erythrocytes with the parallel effect of conditioning to hypoxia and to dynamic loads was the same as in animals subjected only to adaptation to hypoxia. The amount of hemoglobin in these animals was slightly higher than in those who were only adapted ($P>0.01$).

TABLE 1. CHANGES IN THE NUMBER OF ERYTHROCYTES, HEMOGLOBIN AND WEIGHT IN DIFFERENT GROUPS OF ANIMALS BEFORE, DURING AND AFTER ADAPTATION TO HYPOXIA AND CONDITIONING IN RUNNING.

Group	7th day after beginning	3rd day end of effect	Group	7th day after beginning	3rd day end of effect	Group	Before effect	3rd day end of effect
	M	M		M	M		M	M
	Erythrocytes, 1000/lcm^3			Hemoglobin, g%			Weight, g	
DA	5726	6727	DA	14.8	17.8	DA	152	158
DC	5638	5570	DC	14.5	13.9	DC	152	166
A	5642	6540	A	14.2	16.4	A	152	168
C	4960	5000	C	13.1	11.8	C	152	204

Comment: DA are the dynamically adapted animals who have been parallely conditioned to muscular loads and adapted to hypoxia; DC is the dynamic control group of animals who have been conditioned only to dynamic loads; A are the adapted animals who have been adapted only to hypoxia; C is the control group of rats kept under conditions of the vivarium in Moscow.

The number of reticulocytes in the conditioned animals was the same as in the unconditioned animals. Changes in the red blood show that the physical load which we selected was average weight. The heavy physical work caused a decrease in the number of erythrocytes and hemoglobin in the peripheral blood and was accompanied by an increase in the number of reticulocytes.

The number of eosinophils in all groups was almost identical. In animals kept under conditions of the vivarium, somewhat higher numbers were observed but the differences were statistically unreliable.

The weight of the animals subjected both to conditioning only to one of these factors studied by us and those subjected parallelly to both varied identically. All the groups of animals lagged in weight from the control group by 30-40 grams. The differences between the three groups were statistically unreliable. The differences of each of these groups from the fourth are reliable. /96

Thus, conditioning to dynamic loads just as adaptation to hypoxia produced changes in the red blood and a lag in weight of the animals. In spite of the single direction of the changes of the characteristics which we studied, conditioning to dynamic loads gave no increase in tolerance of the rats to acute hypoxia (Table 2).

TABLE 2. LIFETIME OF DIFFERENT GROUPS OF ANIMALS UNDER CONDITIONS OF ACUTE HYPOXIA.

Group *	M, min	P	Group *	M, min	P
DA	12.3	>0.01			
D	6.5	< 0.5	A	15.2	< 0.5
C	7.9	>0.01	DA	12.3	
A	15.2				

* The designations are the same as in Table 1.

As follows from this table the conditioning of animals to dynamic loads not only did not increase the ifetime of the animals at "high altitude", but even lowered it slightly.

The decr ase of thid characteristic was noted both in animals who were conditioned only to dynamic loads in comparison with the control group and in animals who were subjected to the parallel effect of the two factors in comparison with animals who were adapted only to hypoxia.

In conclusion we can say that it is not in all cases that conditioning to physical loads is accompanied by an increase in the tolerance of an organiam to hypoxia. Such an increase was observed with the simultaneous effect of conditioning and adaptation; the isolated effect of only one conditioning to physical loads and even the parallel effect of two of these factors did not lead to an increase in the tolerance of the organism to hypoxia.

THE EFFECT OF PROLONGED STAY UNDER CONDITIONS OF LOWERED BAROMETRIC PRESSURE ON TOLERANCE OF G-LOADS

N.N. Uglova

In experiments on white mice, rats and guinea pigs we studied the effectiveness of the influence of adaptation to hypoxia on the tolerance of transversely directed G-loads. It was established that both an interrupted 14-day pressure-chamber adaptation to hypoxia with evacuation from 528.5 to 307 mm Hg and a 30-day acclimatization under high-altitude conditions (Mt. Elbrus) at an altitude of 2000 - 3800 m produces an increase in the survivability under the influence of G-loads of adapted mice on an average of 25%, in rats of 19%, in guinea pigs of 30%. Here it was noted that the adaptation effect is retained approximately for a period of 3 weeks. Both types of conditioning are accompanied by an increase in the amount of hemoglobin and number of erythrocytes in the peripheral blood of the animals.

A significant amount of research has been devoted to seeking /97 means and methods of increasing tolerance to the effect of G-loads.

A rather high effectiveness has already been established for anti-G-load suits (which have already found use in aviation [1, 8, 13, 26]), for immersion environments [22, 25, 28], for pharmacological compounds [5, 16, 20], for physical conditioning [11, 17] and for several others.

It is known that with a prolonged effect of transversely directed G-loads ane of the leading links in pathogenesis of the approaching disorders is the oxygen starvation of the vital organs and tissues.

At the present time it has been strictly established that conditioning to oxygen deficiency increases the tolerance of the organism to the effect of many environmental factors [2, 4, 12, 23]. Therefore it is feasible to continue the research begun by N.N. Sirotinin [15] on studying the possibility of using adaptation of the organism to hypoxia for increasing tolerance to G-loads.

The problem of this research was to determine the degree of effectiveness of adaptation to hypoxia for the tolerance of animals to transversely directed G-loads and to establish the times of readaptation.

The research was conducted on 730 white mice, 119 white rats and 28 guinea pigs. The experiments were carried out with adaptation of the animals under pressure-chamber and high-altitude con-

ditions. The length of the adaptation under pressure-chamber conditions was 14 days and consisted of daily six-hour sessions at altitudes of: 1st day, 3000 m; 2nd-3rd days, 4000 m; 4th day, 4500 m; 5th-7th days, 5000 m; 8th day, 5500 m; 9th day, 6000 m; 10th-11th days, 6500 m; 12th-14th days, 7000 m. During the adaptation the humidity in the pressure chamber was kept at a level of 50-70% and the temperature at 25-27° C.

Acclimatization under high-altitude conditions was carried out in the region of Mt. Elbrus at an altitude of 2000-3800 m above sea level.

G-loads of 45 units for the white and mice and 25-30 units for the white rats and the guinea pigs were reproduced on a centrifuge with a radius of 4.7 m for the 1st-6th days and 9th-18th days following completion of the adaptation.

Evaluation of the tolerance to G-loads was conducted on the /98
basis of comparing survival in the experimental and the control groups; in the experiments on rats and guinea pigs, furthermore, the character and degree to which the disruptions occured in heart function were analyzed from data of the electrocardiogram and change in respiration.

For the purpose of studying the dynamics of the acclimatization process in the experimental animals we periodically determined the amount of hemoglobin, the erythrocytes and reticulocytes in the peripheral blood, the oxygen requirement and the body weith. Here we established the following: the increase in the number of erythrocytes in the white mice subjected to the pressure chamber increased maximally to 3,450,000; in the white rats to 1,260,000 and in the guinea pigs to 800,000. The hemoglobin increased by 5, 1.4 and 0.6 g%, respectively. The increase in the erythrocytes in the white mice, subjected to an altitude of 3800 m, equaled 125,000; in the rats it was 780,000 and in the quinea pigs, 350,000. The increase in hemoglobin did not exceed 2.6 g%. These results agree with the literature data [9, 14, 18-21, 27]. With equivalent conditions of volume and feeding the weight of the animals varied differently. As a rule, a large increase in weight was observed in the control animals. The experimental mice, rats and guinea pigs, if they had an increase in weight, had a gain that was less than that of the control animals.

The gaseous metabolism of the animals adapted both to pressure chamber conditions and those of high altitude, had a slight tendency to decrease, however, the differences in statistical interpretation were found to be insignificant. Analogous results were obtained also by other authors. Thus, according to the data of Kreps et al the gaseous metabolism of the "hypoxic" rats at rest (in an environment of atmospheric air) did not differ from that of the control animals [10].

In analyzing the cardiac activity almost in all experiments during the time of the G-load effect, bradycardia set in significantly earlier and deeper in the control rats and guinea pigs, as shown by the collapse of the compensatory mechanisms (Fig. 1). With the beginning of rotation, an increase in respiration was observed. However with a G-load of 15 - 20 units, difficulty developed in the respirational movements and on the curves of registering the perimeter of the chest a flat line was often recorded (Fig. 2). In the period of recovery in the majority of cases an expressed compensatory shortness of breath was observed. Here no pronounced differences were noted in the change in breathing between the control and the experimental animals.

The tolerance of the animals to the effect of G-loads was most distinctly expressed during the first rotation in the centrifuge conducted on the 1st - 6th days following adaptation (Table 1).

From the data cited, it is clear that in all experimental groups, without exception, the survival was greater than in the control animals. Thus the survival of the adapted white mice exceeded that among the control animals by 28.1% (t = 5.3); and in the rats, by 19.5% (t = 1.96). /99

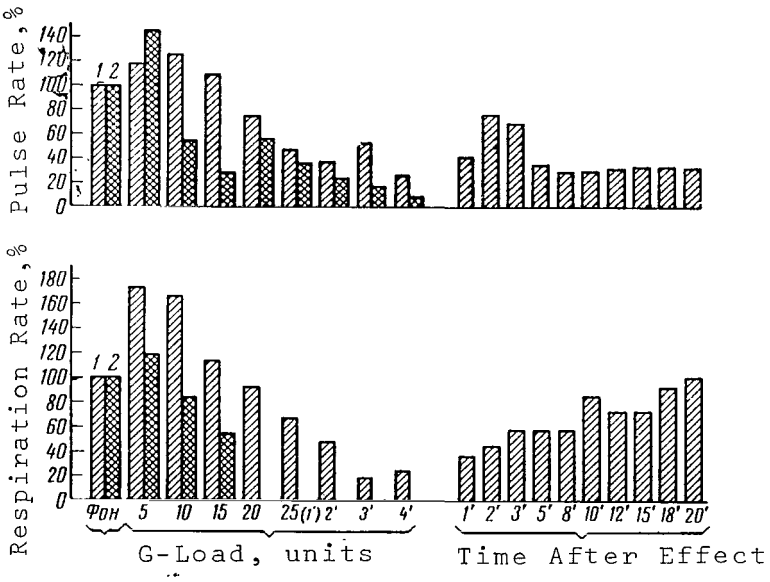

Fig. 1. Dynamics of the Pulse and Breathing Rate in Adapted (1) and Control (2) Guinea Pigs Acted on by G-Loads.

A similar picture was observed during rotation of the animals acclimatized under high-altitude conditions (Table 2). In the mice the difference in survival during the times of the test reached 23.5% (t = 1.91) and in the guinea pigs, 30% (t = 1.4).

With the action of the G-loads on the 9th - 18th days after completetion of the adaptation the difference in survival was already less contrasting, i.e., a gradually approaching loss was observed in the increased tolerance of the animals adapted to hypoxia. On the 28th day the increased tolerance to G-loads, as we reported previously [7], was retained only in the animals who had undergone active acclimatization (hypoxia + physical conditioning). It is interesting that in animals who were adapted under pressure-chamber conditions more expressed changes were observed from the side of the characteristics of the red blood; they possessed somewhat higher tolerance to G-loads and lost them later than the mice and the rats acclimatized (without physical load) at high altitude.

A lower degree of acclimatization effect in the animals conditioned under high-altitude conditions is explained apparently by the fact that the maximal evacuation in the mountains was only 474 mm Hg (3800 m), whereas in the pressure chamber it was equal to 307 mm Hg (7000 m).

/100

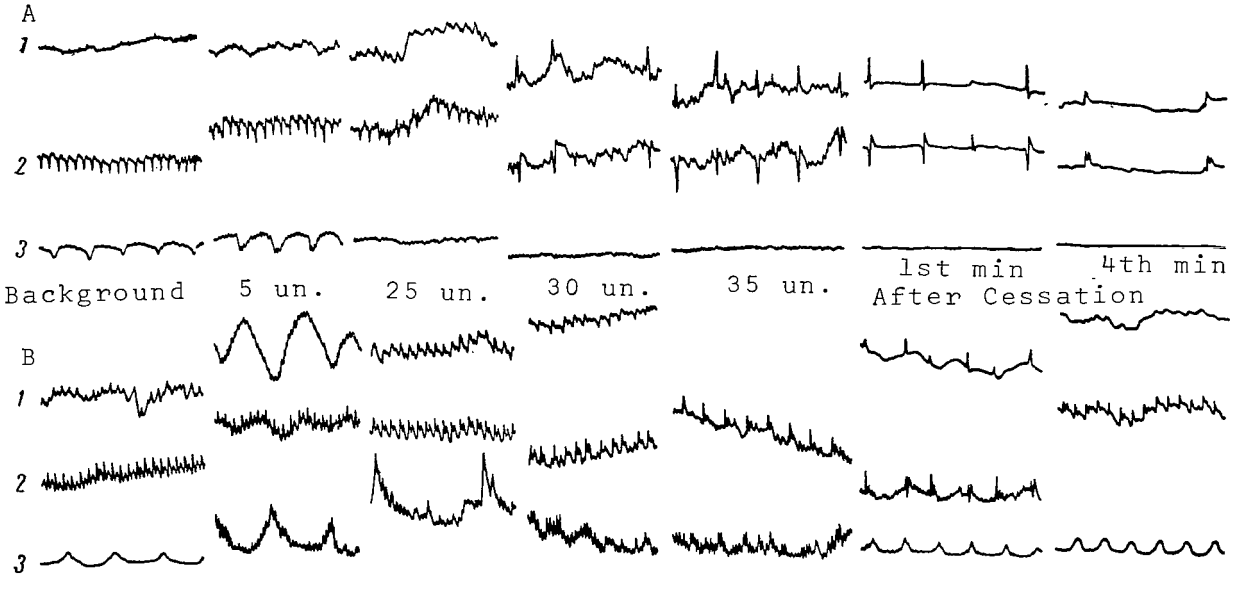

Fig. 2. Change in the EKG and Respiration in Control (A) and Adapted (B) White Rats Acted on by G-Loads. 1. EKG, Lead I; 2. EKG, Lead II; 3. Pneumogram.

TABLE 1. SURVIVAL OF CONTROL ANIMALS AND THOSE ADAPTED TO HYPOXIA UNDER PRESSURE-CHAMBER CONDITIONS ACTED ON BY G-LOADS. /101

Animals	Group	Number of Animals	Days of Rotation in Centrifuge	Result		Survival, %
				Died	Lived	
Mice	Control	141		85	56	39.7
	Adapted	140	1 - 6	45	95	67.8
	Control	113		69	54	47.7
	Adapted	151	9 - 18	64	87	57.6
Rats	Control	40		29	11	27.5
	Adapted	49	1 - 6	26	23	47
	Control	15		11	4	27
	Adapted	15	9 - 16	8	7	47

TABLE 2. SURVIVAL OF CONTROL ANIMALS AND THOSE ACCLIMATIZED TO HYPOXIA UNDER HIGH-ALTITUDE CONDITIONS ACTED ON BY G-LOADS.

Animals	Group	Number of Animals	Days of Rotation in Centrifuge	Result		Survival, %
				Died	Lived	
Mice	Control	48		29	19	39.9
	2100 m	47	4	25	22	46.8
	3800 m	30		11	19	63.4
	Control	20		14	6	30
	2100 m	20	15	13	7	35
	3800 m	20		15	5	25
Guinea Pigs	Control	10		6	4	40
	Acclimatized	10	5 - 14	3	7	70
	Control	4		4	0	0
	Acclimatized	4	28	4	0	0

Thus, in the experiments on the various types of animals, we believe it has been definitely proven that a favorable effect of adaptation to hypoxia is exerted on the tolerance of G-loads. These data are confirmed by subsequent research carried out in our laboratory on humans [6].

Analysis of the results of these investigations and comparison of them with clinical-physiological reactions to the effect of hypokinesis and weightlessness (decrease in the mass of the circulating blood, plasma loss, decrease in the number of erythrocytes and the hemoglobin, deterioration in the blood supply of a number

of organs and tissues, decrease in the muscular tonus and the overall tolerance to forces of gravity) permit us to assume that the use of hypoxia may be an effective method of maintaining high tolerance of the organism of astronauts under conditions of prolonged flight. /102

Proceeding from the similar character of the reactions of the organism to hypodynamia and hypoxia, L.E. Lemb arrives at analogous recommendations for pilots of space craft [24].

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THE EFFECT OF PRELIMINARY INTERRUPTED STAY IN A RAREFIED ATMOSPHERE ON THE TOLERANCE OF RATS TO TRANSVERSE G-LOADS

V.G. Petrukhin

ABSTRACT: For a period of 23 days (all day) white rats were placed in a rarefied atmosphere (altitude of 4500 - 500 m) after which they were subjected to the effect of transverse G-loads. The conditioned rats showed a higher level of tolerance to transverse G-loads. We found in them a statistically reliable increase in the relative weight of the adrenal glands and heart, hemorrhages were more often encountered in the lungs, glycogen was retained in large amount in the liver; dystrophic and necrobiotic changes in the muscular fibers of the myocardium were found in a smaller amount than in the unconditioned animals. Favorable effects of conditioning were an increase in the tolerance of the organism to insufficient supply of oxygen to the tissues and an improvement in the oxygen supply to the vital organs as well as an increase in erythropoiesis and an increase in the ability of the myocardium to carry on physical work that was greater than prior to the experiment.

One of the causes of the physiological and morphological /103
changes in the organism acted on by large and prolonged G-loads is hypoxia. During the time of the G-loads, due to these different causes, there occurs an oxygen debt of the organism and in the arterial blood the amount of oxygen is decreased in comparison to the original level.

Among the basic factors which produce disruption in the activity of the heart, a very large role is played by physical overexertion of the myocardium and change in the vascularization of the organ. More often a combination of these factors is observed. In both instances, with an insufficiency of the adaptation and compensatory possibilities of the organism, the immediate reason for the occurrence of biochemical and then the destructive disruptions of the heart is hypoxia of the myocardium. For some time now conditioning of the organism to hypoxia has been used to increase the adaptation and compensatory possibilities of the organism acted on by the factors causing a deficiency of oxygen to the myocardium.

Numerous investigations have established that such conditioning, accomplished with the aid of high-altitude ascents by periodic

residence in a pressure chamber with a rarefied atmosphere, increases the tolerance of the organism not only to the rarefied atmosphere but also to other harmful effects such as, for example, radiation illness [2, 3, 4, 8, 12, 13, 15-18, 20-22]. An organism that is conditioned to hypoxia can tolerate somewhat better deep /104
hypothermy, physical load and other stress effects: cold, heat, etc. [9-11, 14, 19, 23].

The most convenient method of adapting to conditions of oxygen starvation is the placement of animals into a pressure chamber with a rarefied atmosphere. Conditioning to hypoxia occurs after the animal remains at an altitude of 5000 - 7000 m for 4 - 5 times for a period of even two hours [8].

In this research we have used adaptation to conditions of oxygen starvation as a means of increasing tolerance to the effect of transverse G-loads.

For the experiment we took 20 white male rats of the same age and approximately the same weight. The animals were divided into two different groups. The first group (experimental) every other day was placed for a day into a pressure chamber where the air was evacuated so that it corresponded to an altitude of 4500 - 500 m. The concentration of carbon dioxide in the pressure chamber did not exceed 1 - 1.5%. The second group (control animals) for this same time was placed alongside of the pressure chamber. Feeding and handling were the same. In all, for 45 days, 23 sessions were conducted, i.e., the experimental animals were subjected to high altitude for 23 days. The conditioning was conducted by I.R. Kalinichenko. No changes in the behavior or lowered appetite in the experimental animals were noted.

After three days following end of the conditioning each experimental and control rat was placed in a box with a protective lining. The boxes were attached to the wheel of the centrifuge so that during rotation G-loads were produced on the rats that were directed from the spine toward the chest (the rats were pressed to the protective lining by centripetal force). The experimental and the control animals at the same time were subjected to the effect of 13-fold G-loads for a period of 20 minutes. After the G-loads all the rats were sluggish and only slightly mobile; they could not even climb out of the box. After 5 - 10 minutes their activity was restored and then they differed in behavior not at all from the ordinary animals.

One rat, who was not subjected to preliminary conditioning in the pressure chamber (control) died during the time of the G-loads. We found in him confluent hemorrhages in the diaphragmatic parts of both lungs and punctate hemorrhages in the other parts. The liver, the kidneys and the brain were plethoric. Almost no glycogen was in the liver.

The rats that survived were killed at different times following the G-loads: after 10-15 minutes, 4 hours, 1,3,7 days. After weighing the organs, parts of the brain, the heart, the lungs, the liver, the adrenal glands and the kidneys were placed into a Karnua mixture and in a 10%- solution of formalin. All the cross-sections were colored with hematoxylin-eosin. To find the amount of glycogen (in the myocardium and liver) we used the Shabadash method, for the amount of fat we used a dye of sudan black, for the amount of cholesterin (in the adrenal glands) we used a polarization microscope and for the ribonucleic acid (in the adrenal glands) /105
we used the Brashe method. The cross-sections of the myocardium were furthermore colored with ferric hematoxylin after Geydengayn (to find the albumino-mass degeneration) and after Sel'ye to find the fuchsinophil degeneration. The cross-sections of the brain were studied after Nisslyu.

In the experimental animals, in comparison with the control animals, we found a statistically reliable increase in the relative weight of the adrenal glands and an unreliable increase in that of the heart.

Pathologo-morphological changes in the organs after the effect of G-loads both in the experimental and the control rats, as a function of the time of change was characterized by a disruption in the blood circulation and the appearance of hemorrhages, by a decrease in the glycogen reserves, by an increase in the functional stress of the adrenal glands and by the development of dystrophic, inflammatory and necrobiotic changes in the parenchymal organs. However, the level of G-load tolerance in the animals who were preliminarily subjected to conditioning to hypoxia was higher than in the unconditioned rats. This is shown by the large number of changes in the organs found in the control animals adapted to the same G-load as the experimental adapted rats. Of eight animals who were killed in the course of the first days after the effect of the G-loads hemorrhages in the lungs of the control animals were encountered five times including two rats who had confluent hemorrhages. In the conditioned animals punctate hemorrhages were found only in one. Of the four control animals killed after three and seven days, focal pneumonia which developed at the site of the hemorrhages was found in three rats and in the experimental animals only one (Fig. 1). In the control rats, killed after 10 - 15 minutes following the G-loads, the amount of glycogen in the liver was less in comparison with the experimental conditioned animals.

The majority of structural changes that occurred from the G-loads appeared best of all three days following the experiment; by the seventh day an almost complete recovery of the structure of the organs had occurred. In the control animals, killed during these times, in the myocardium most often there were encountered fibers which had undergone vacuolar dystrophy (Fig. 2). Segments were found im them in a large amount with indications of albuminous

Fig. 1.

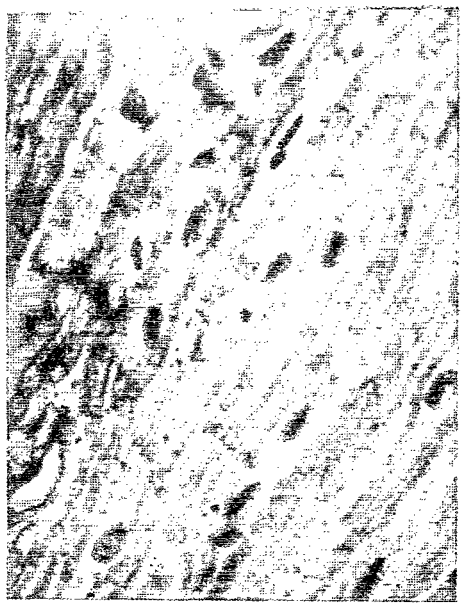

Fig. 2.

Fig. 1. Focal Pneumonia in an Unconditioned Rat, Killed Three Days Following G-Loads. The Alveolae Surrounding the Bronchus were Filled with Edematous Fluid, Leukocytes and Degenerating Erythrocytes - the Focal Point of Bronchial Pneumonia. Hematoxylin-Eosin, 630 X.

Fig. 2. Mycardium (Interventricular Septum) of an Unconditioned Rat, Killed One Day Following G-Loads. In the Majority of Muscular Fibers Around the Nucleus is an Optically Empty Space Consisting of Fused Vacuoles - Vacuolar Dystrophy. Hematoxylin-Eosin, 630 X.

dystrophy, manifested in the form of a loss in the transverse and longitudinal lines, an increase in the colorability of the sarcoplasm with eosin, the appearance of fuchsinophil degeneration (after Sel'ye) and an albumino-mass degeneration (Fig. 3). And in two of the unconditioned animals we even found necroses in parts of the muscular fibers with the reaction of the stroma of the myocardium in the form of a multiplication of the endomysial elements (Fig. 3), which was never encountered in the experimental, conditioned animals.

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Fig. 3.

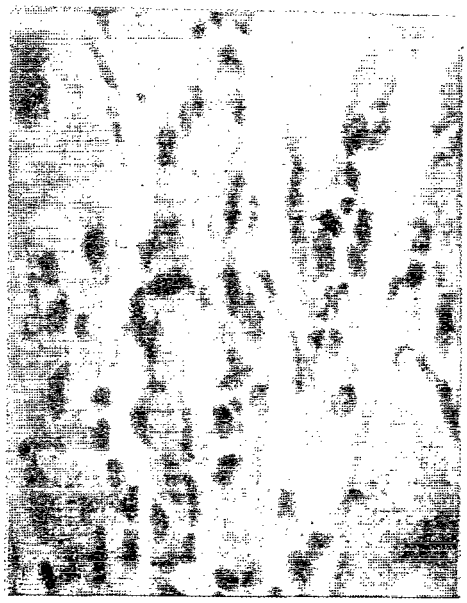

Fig. 4.

Fig. 3. Myocardium (Left Ventricle) of a Rat Unadapted to Hypoxia, Killed One Day Following G-Loads. Mass Degeneration of the Individual Muscular Fibers. Ferric Hematoxylin, after Geydengayn, 460 X.

Fig. 4. Myocardium (Interventricular Septum) of a Rat Unadapted to Hypoxia, Killed Three Days Following G-Loads. Multiplication of the Endomysial Cells at the Site of the Degenerating Muscular Fibers. Hematoxylin-Eosin, 630 X.

Changes in the kidneys were limited to plethora in the rats, killed prior to one day following the G-loads. In the adrenal /108
glands we found a significant decrease in the lipids and the cholesterin in the protoplasm of the epithelial cells of the lower and middle third of the nodular zone. In the liver of the animals killed immediately following the G-loads we observed a marginal standing of the leukocytes in the septal capillaries dilatated with blood and then vacuole dystrophy developed which disappeared by the third day of observation. In the brain, other than a small perivascular edema, no chromatolysis or vacuolozation of the individual ganlionic cells or other changes were noted. The described changes were noted. The described changes in the kidneys, liver, brain and adrenal glands however often and almost in the same amount

were encountered both in the experimental and in the control animals. In the animals conditioned to hypoxia we noted a somewhat larger degree of pyroninophilia of the protoplasm of the cells of the cortical material of the adrenal glands. The increase in the amount of ribonucleic acid with a lowering in the amount of cholesterin and lipids, as we know, indicates an increased functional activity of the adrenal cortex.

The positive effect of conditioning animals to hypoxia for tolerance of transverse G-loads deserves fundamental attention and requires further study. However, this effect is not an unexpected one. It is caused by the increase in tolerance of the organism to an insufficient supply of oxygen to the tissues and to an improvement in the oxygen supply to the vital organs, in particular to the central nervous system and the heart. The increase in erythropoiesis and the increase in the ability of the myocardium to carry out physical work, that is greater than in the experiment, are of great significance in increasing tolerance.

Data on the positive effect of conditioning to hypoxia for tolerance of animals to G-loads agree with the interesting investigations of P.V. Vasil'yev and his associates who conducted conditioning of persons and animals both under high-altitude and pressure-chamber conditions [5,6]. In the humans, after acclimatization, the tolerance to transverse G-loads was increased on the average by 2 units. P.V. Vasil'yev and N.N. Uglova, in experiments on animals, showed that active acclimatization under high-altitude conditions is most effective, when it includes simultaneously the effect of hypoxia and moderate physical load [7].

CONCLUSIONS

1. The tolerance level to transverse G-loads of animals preliminarily subjected to hypoxic conditioning is higher than in ordinary unconditioned rats.

2. Under the influence of transverse G-loads in conditioned animals hemorrhages in the lungs occur more seldom, glycogen is retained in a large amount in the lever and dystrophic and necro- /109
biotic changes in the muscular fibers of the myocardium are developed in a lesser amount than in the unconditioned rats.

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THE EFFECT OF ADAPTATION TO CONDITIONS OF A CHANGED GASEOUS ENVIRONMENT ON TOLERANCE TO G-LOADS

P.V. Vasil'yev and N.N. Uglova

ABSTRACT: In this article we cite experimental data on the results of investigating white mice and rats in a study of the influence of prolonged stay under conditions of changed gaseous environment on tolerance of the organism to G-loads. Here it was shown that breathing for 6 hours a day for a period of 14 days of a hypercapnic gas mixture (5 - 12% CO_2) does not substantially change tolerance to G-loads (there is a tendency toward an increase), but breathing a hypoxic mxiture (up to 3.6% O_2) or a hypoxic and hypercapnic mixture increases it significantly. It was established that hypercapnia slows down the erythrocytic reaction to oxygen deficiency. A suggestion is made concerning the possible physiological mechanisms of these peculiar reactions.

The problem of increasing the tolerance of the organism to the effect of G-loads, with the beginning of space navigation, is now one of reality. Solving this problem can be done by various means, among which adaptation to hypoxia is a very important one. This means of investigation is based on analysis of the pathogenetic /110 mechanisms of all disorders which are developed under the influence of G-loads.

As we know from the research of a number of Russian and foreign authors, the most important link in the pathogenesis of disorders observed under a prolonged G-load effect, is the hypoxic and circulatory forms of oxygen starvation [1, 2, 6, 11, 13, 18, 19, 21, 30-34, 43]. Therefore even in the first research carried out on the effect of G-loads on animals adapted to hypoxia, the favorable effect of this nonspecific method of increasing tolerance of the organism to G-loads was clearly revealed [7-9, 15, 24, 27, 28, 38]. All this research on adaptation to hypoxia was conducted by the authors mainly with lowered barometric pressure of the air under pressure-chamber of high-altitude conditions.

In the literature available to us, we were unable to find any work on the effectiveness of adaptation to hypoxia as a means of increasing tolerance to G-loads with breathing of gas mixtures having a depleted amount of oxygen. However, there do exist several reports on increasing tolerance to acute oxygen starvation of adapted animals and man with breathing of air having a low oxygen content [29].

Of significant interest is a study of the effect of prolonged residence of the organism in a gaseous environment having an increased amount of CO_2 on its tolerance to G-loads. There exist data in the literature which indicate a favorable effect of comparatively short-term breathing of a gas mixtures with an elevated amount of carbon dioxide on tolerance to anemia of the brain, hypoxia, hyperoxia, hypercapnia and G-loads [14, 22, 23, 26, 35, 36]. On the contrary, according to the data of V.P. Zagryadskiy and associates, a two - four hour residence of animals and man in a gaseous environment with a carbon dioxide content from 1.5 to 5% lowered tolerance to high temperature, breathing under excess pressure, physical load and G-loads [16, 17].

With flights in space craft, for a number of reasons emergency conditions may occur with sharp changes in the gas composition with respect both to oxygen and carbon dioxide.

Procedding from the above, the problem of this paper was to study the ffect of a changed gaseous atmosphere on the tolerance of the organism to G-loads and to explain the possibility of using this method for raising the nonspecific tolerance of the organism.

METHOD

The investigation were carried out on 282 white mice and 15 /111
rats in three series of experiments:

Series 1: Adaptation under conditions of a changed gaseous atmosphere with interrupted, gradually increasing hypercapnia;

Series 2: Adaptation under conditions of a changed gaseous atmosphere with interrupted, gradually increasing hypoxia;

Series 3: Adaptation under conditions of a changed gaseous atmosphere with interrupted, gradually increasing hypoxia and hypercapnia.

The composition of the gas nixtures and the time of residence in them during the time of adaption are given below in the description of the results of the investigations.

During the time of the adaptation the animals were placed into a special chamber, in which a gas mixture was supplied from tanks prepared utilizing a dosimeter used in the devices of gas narcosis. A constant control over the gas composition in the chamber was carried on by connecting a complex gas analyzer form the firm Godart. The overall schematic of the set up is shown on Figure 1.

We used silica gel as the mositure absorbent, placed in various departments of the chamber.

In each series the animals were distributed into experimental /112

(adaptable) and control groups. In all groups the animals were not given food or water round the clock.

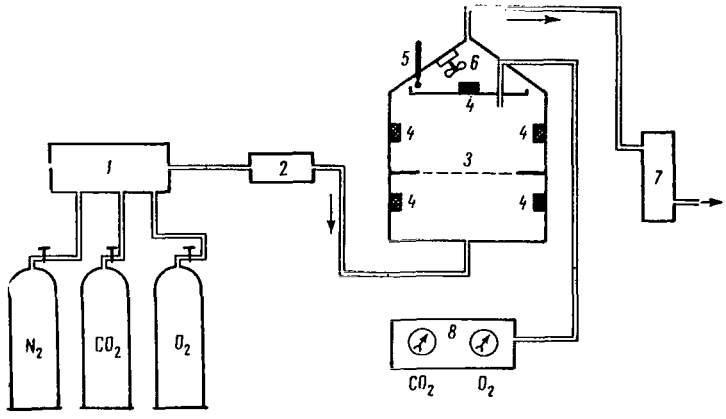

Fig. 1. Schematic of the Set Up for Adaptation of Small Animals to Conditions of a Changed Gaseous Atmosphere. 1. Dosimeter; 2. Rotameter; 3. Chamber for the Animals; 4. Silica Gel; 5. Thermometer; 6. Ventilator; 7. Water-Jet Suction Pump; 8. Gas Analyzer.

Before adaptation, during adaptation and during the period of readaptation the amount of hemoglobin, the number of erythrocytes, reticulocytes and eosinophils were determined in part of the experimental and control mice and in all of the rats. They were weighed during these times.

On the 3rd-17th days after adaptation we determined the tolerance of the animals in the experimental and control groups to the effect of transversely directed G-loads reproduced on a centrifuge with a raduis of 4.2 m for the rats and 4.7 m for the white mice.

During the time of rotation the white mice were placed into plywood boxes, divided into individual sections. In each section one animal was placed. The rat was held on his back in special chutes and three were rotated simultaneously: one control rat and two adapted rats. An EKG was recorded for all rats during the time of rotation.

The gradient in increase and decrease of G-load was 1 unit/sec^2. The value of the G-load for the mice was 45 units, twice for 10 minutes (the interval between the first and second rotation was 10 minutes); for the rats the initial value of the G-load was 20 units for a period of 1 minute, with a subsequent gradual increase to 5 units until deep disorders occured in the cardiac activity on one of the three rotating animals.

The overall evaluation of the effectiveness of adaptation was carried out on the basis of the survival and the character of the changes in cardiac activity.

RESULTS

The first series of experiments on studying the effect of adaptation to carbon dioxide for the tolerance of animals to G-loads was conducted on 108 white mice: 54 of the animals served as a control and were kept under ordinary conditions of the vivarium and 54 were subjected to gradual adaptation to an increased amount of CO_2 in the inhaled air.

The dynamics of the increase in carbon dioxide by day appared in the following manner: 1st-5th days, 1.5 $\pm$ 0.5%; 6th-12th days, 3.0 $\pm$ 1.0%; 13th-17th days, 5.0 $\pm$ 1.0%, 18th-21st days, 10.0 $\pm$ 1.0%; 22nd-27th days, 12.0 $\pm$ 1.0%.

The amount of oxygen in the inhaled gaseous mixture was maintained at a level of 20 $\pm$ 1.0%, and the temperature of the air in the chamber varied from 22 to 25° C. Each day, other than Sundays, the animals were subjected to these conditions from six to eight hours.

On the third day following completion of the adaptation to the gaseous mixture with 5, 10 and 12% CO_2 content, the mice from the experimental and control groups were subjected to the effect of G- /113
loads under the above conditions in order to determine their tolerance.

The overall behavior of the animals at all concentrations of carbon dioxide used before, during and after the experiment was ordinary with the exception of distinctly expressed dyspnea, especially with a high CO_2 content in the inhaled mixture, At the beginning of each exposure with 10 and 12% carbon dioxide many of the animals assumed the position of "bedouins", carrying out in this case washing motions with the forepaws. However after 30-40 minutes, the greater part of the mice became immobile; the animals came together in one group, being fully occupied with one another and by the end of residence in the chamber were found in a state of well-expressed general slow down and somnolence. They took almost no food and water during this time.

A significant lag in body weight increase was observed in the experimental mice. Thus, in the adapted animals by the 30th day following the beginning of the experiment the weight was increased in all by 6.4% with respect to the original, but in the control animals by 19.5%.

The dynamics of changes in the investigated characteristics of the peripheral blood, taken from an incision at the end of the tail, are shown on Table 1 and in Figure 2.

TABLE 1. CHANGE IN BLOOD IN WHITE MICE DURING THE TIME OF ADAPTATION TO HYPERCAPNIA. (AVERAGE DATA).

Characteristic	Original Data	Days of Adaptation 11	17	21	27
Hemoglobin, g%	13.2±0.2	12.9±0.23	13.7±0.21	12.6±0.36	11.9±0.32
	n=40	n=10	n=10	n=10	n=10
Erythrocytes, 1000	8580±166	9870±490	8980±248	8995±437	9255±376
	n=40	n=10	n=10	n=10	n=10
Reticulocytes, 0/00	13±1.3		11.3±1.2		19.6±4.6
	n=36		n=9		n=9

Comment: n = number of animals tested.

From the data cited it s obvious that the mount of hemoglobin in the adapted mice not only id not increase but even had a tendency to decrease; the number of erythrocytes and re iculocytes increased slightly, especially on the 11th and 17th days of the experiment. During these days the increase in the erythrocytes reached 15%, and the reticulocytes, 50%. However the probability of error only on the 11th day for the erythrocytes and on the 27th day for the reticulocytes did not exceed 5% ($t \geq 2.5$); in all the other /114 cases the differences were found to be statistically unreliable ($t \leq 1.6$).

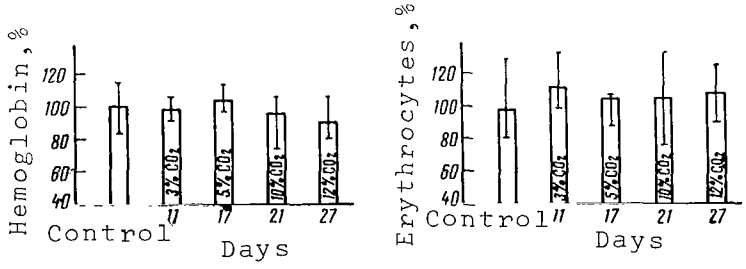

Fig. 2. Amount of Hemoglobin and Number of Erythrocytes in the Blood of White Mice During their Residence in a Hypercapnic Mixture in Percent of the Original Level. The Lines Show the Individual Deviations form the Mean Value.

In determining the G-load tolerance a sligh increase in survival in comparison with the control animals was observed only after adaptation iwth 10 and 12% CO_2 (Fig. 3). But the probability of

randomness in the differences (after Fisher's method) in these experiments was > 0.025, which prevents us from sssuming the observed difference is reliable. Consequently, adaptation to hypercapnia under these conditions does not show a positive effect on the tolerance of the organism to the effect of G-loads.

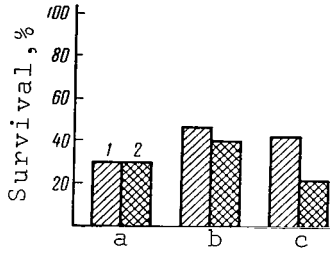

Fig. 3. Survival of Experimental (1) and Control (2) Mice Acted on by a G-Load of 45 Units on the Third Day Following Completion of the Adaptation. a. Adaptation with a Gaseous Mixture Content of 5% CO_2; b. 10%; c. 12%.

The second series of experiments was carried out on 107 white mice (51 mice in the control group and 56 in the adapted group) and 15 male rats weighing from 150 to 180 g (5 in the control group and 10 in the adapted group) to investigate the effect of adaptation to conditions of depeleted O_2 in the gaseous atmosphere on the tolerance to G-loads. The decrease in the partial oxygen pressure in the air corresponded approximately to the degree of its rarefication during the 12-day acclimatization under pressure-chamber conditions. The decrease in the partial pressure of O_2 was compensated by the increase of nitrogen in the gaseous mixture. The amount of carbon dioxide did not ecxeed 1.0%.

The dynamics of the decrease in oxygen by day in the inhaled /115
gaseous mixture was: 1st day, 13.6%; 2nd day, 12.7%, 3rd-4th days, 11.9%; 5th-6th days, 11.2%; 7th day, 10.2%; 8th-9th days, 9.8%; 10th day, 9.2%; 11th-12th days, 8.6%.

The temperature of the air in the chamber at the beginning of the experiment was equal to 19-21°, and at the end to 28 ± 2° C. The daily time of adaptation continued for six to eight hours. T e conditions of the vivarium were maintained and the supply in all groups of animals was identical and precisely the same as in the previous series of experiments.

In weighing the mice and rats a lag in weight of the adapted animals was distinctly clear. In fact, on the day of completion of the adaptation the weight of the control mice was 116 and that of the rats 114% of the original; the weight of the experimental animals was respectively equal to 109 and 107%.

The dynamics of changes in the blood in adapted mice are shown in Table 2.

TABLE 2. CHANGE IN THE CHARACTERISITICS OF THE BLOOD DURING THE TIME OF ADAPTATION TO HYPOXIA UNDER CONDITIONS OF AN ATMOSPHERE DEPLETED OF OXYGEN (AVERAGE DATA).

Characteristic	Original Data	Days of Adaptation	
		5	12
Hemoglobin, g%	13.4±0.27 n=20	14.3±0.29 n=10	15.4±0.22 n=10
Erythrocytes, 1000	8251±202 n=20	8580±601 n=10	10580±268 n=10
Reticulocytes, 0/00	31.4±2.6 n=19	37±2.9 n=10	34±2.4 n=10

From the data presented in Table 2 it is clear that the common law consists of increase in the amount of hemoglobin and erythrocytes in adapted mice, accompanied simultaneously by moderate reticulocytosis.

With statistical processing of the data it was shown that the probability of error of the compared characteristics does not exceed 5% ($t > 1.96$).

Analogous results have been obtained also in experiments on white rats (Table 3). In analyzing the blood, eosinopenia appeared which indicates the physiological stress of the functional systems of the organism during the period of adaptation to hypoxia.

It should be noted that both with the control investigations and during the time of adaptation in the animals there were observed significant individual differences in the studied characteristics that are clearly shown on Figure 4.

Determination of the tolerance to G-loads of experimental and control animals was carried out on the 4th, 10th and 17th day following end of the adaptation.

The experimental results are shown on Table 4 and Figure 5.

From the table it is clear that the adaptation of the white rats to hypoxia increased survival by two times. This is confirmed also be experiments on white mice (Fig. 5).

Here there were especially demonstrative differences in the experiments carried out on the 10th day following adaptation. The

TABLE 3. CHANGE IN THE BLOOD CHARACTERISTICS IN WHITE RATS DURING ADAPTATION TO HYPOXIA AND UNDER CONDITIONS OF A GAS ENVIRONMENT DEPLETED OF OXYGEN (AVERAGE DATA). /116

Characteristic	Original Data	Days of Adaptation 5	Days of Adaptation 11
Hemoglobin, g%	$\frac{12,7 \pm 0,42}{n=8}$	$\frac{14,3 \pm 0,26}{n=5}$	$\frac{14,8 \pm 0,3}{n=9}$
Erythrocytes, 1000	$\frac{6400 \pm 248}{n=8}$	$\frac{5670 \pm 95}{n=5}$	$\frac{6950 \pm 210}{n=9}$
Reticulocytes, 0/00	$\frac{5,0 \pm 0,42}{n=8}$	$\frac{24,0 \pm 3,24}{n=5}$	$\frac{16,0 \pm 2}{n=9}$
Eosinophils, units	$\frac{183 \pm 36,9}{n=8}$	$\frac{67 \pm 17,1}{n=5}$	$\frac{115 \pm 11,7}{n=9}$

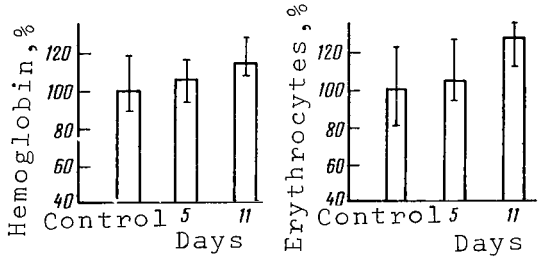

Fig. 4. Change in the Hemoglobin and Erythrocytes in White Mice to the Effect of a Gaseous Environment with Lowered Partial Oxygen Pressure. The Designations are the Same as in Figure 2.

survival in the experimental group of mice was 48.5% greater than in the control group ($P < 0.010$).

The third group of experiments on studying the effect of adaptation to conditions of gradually increasing hypoxia and hypercapnia on the tolerance to G-loads was carried out on 66 white mice; out of these, 26 animals were control animals and 40 were adapted to the complex effect of hypoxia and hypercapnia. To investigate the reaction of the blood we used additionally 2 guinea pigs. /117

The dynamics of the amount of oxygen in the inhaled mixture were precisely the same as in the second series of experiments. The amount of CO_2 on the 1st - 3rd days was kept at a level of 3 $\pm$ 0.5% and on the 4th - 13th days at 5 $\pm$ 1%. The maximal temperature of the air in the chamber was 28 $\pm$ 2°C.

TABLE 4. SURVIVAL OF EXPERIMENTAL AND CONTROL RATS ACTED ON BY G-LOADS ON THE FOURTH DAY FOLLOWING ADAPTATION.

Group	Number of Rats in the Group	Results		Survival, %
		Died	Lived	
Control	5	3	2	40
Experimental	10	2	8	80

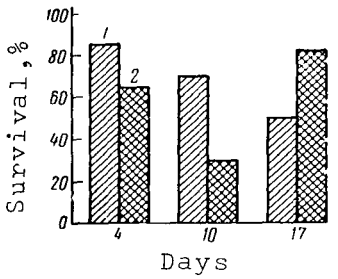

Fig. 5. Survival of Adapted and Control Mice Acted on by G-Loads Following Adaptation Under Conditions of a Gas Environment Depleted of Oxygen. The Designations are the Same as in Figure 3.

The overall behavior and the condition of the mice did not differ substantially from the control animals. Unlike the previous series of experiments in which growing animals were used (original weight 21 - 24 g), in this experiment the experimental and control groups were composed of "mature" animals with a weight of 27 - 32 g (average weight 29 g).

This feature was expressed in the character of the change in weight during the time of adaptation. In the previous series the experimental mice lagged only in weight increase but in this experiment we observed a real decrease in weight. Thus, the weight of the control animals at the end of adaptation was equal to 107.5 and that of the experimental animals to 90.5% with respect to the original.

The reaction of the blood to the complex effect of hypoxia and hypercapnia is clear from the data in Table 5.

From analysis of the data in Table 5, it is clear that the /118
number of erythrocytes and the amount of hemoglobin in the experimental animals did not vary substantially ($t < 1.3$) but the number of reticulocytes on the 13th day from the beginning of adaptation was even lowered from 29 to 18 0/00; these differences are statistically reliable ($t > 2.8$).

TABLE 5. CHANGES IN THE AMOUNT OF HEMOGLOBIN, THE ERYTHROCYTES AND RETICULOCYTES IN THE PROCESS OF ADAPTATION TO THE COMPLEX EFFECT OF HYPOXIA AND HYPERCAPNIA.

Characteristic	Original Data	Days of Adaptation	
		7	13
Hemoglobin, g%	$\frac{13,1\pm0,42}{n=9}$	$\frac{13,5\pm0,21}{n=10}$	$\frac{14\pm0,43}{n=10}$
Erythrocytes, 1000	$\frac{9190\pm260,8}{n=19}$	$\frac{8900\pm210}{n=10}$	$\frac{9180\pm510}{n=10}$
Reticulocytes, 0/00	$\frac{29,0\pm3,7}{n=20}$	$\frac{25,6\pm2,0}{n=10}$	$\frac{18,0\pm1,8}{n=10}$

Analogous results in investigating the blood were obtained also in the experiments on guinea pigs; the amount of hemoglobin in them did not change but the number of erythrocytes in both animals was lowered slightly (to 180,000 and 250,000 per mm^3). The number of eosinophils before adaptation was 448 and 312, but by the end of the experiment it was 168 and 12 respectively.

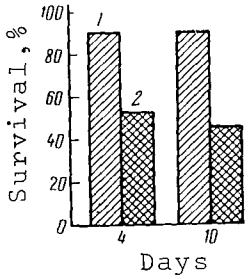

Fig. 6. Survival of White Mice, Adapted Under Conditions of a Gaseous Environment with an Elevated Amount of CO_2 and a Lowered Amount of O_2 Acted on by G-Loads. The Designations are the Same as in Figure 3.

Determination of the Tolerance to G-loads was carried out on the 4th and the 10th days following end of the adaptation (Fig. 6). Here the survival in the experimental group by the 4th day was greater by 37% than in the control group ($P < 0.010$), and by the 10th day, by 44.7% ($P < 0.025 - 0.011$).

DISCUSSION

By analyzing the results of these investigations, we note /119
first of all that the adaptation to conditions of a gas environment with lowered partial oxygen pressure is an effective method of increasing tolerance of the organism to the effect of G-loads. In fact, the survival in adapted groups in the investigations for the period of the first 10 days in the second series of experiments was 20 - 48.5 and in the third group, 37 - 44.7% greater than in the control group. The time of retention of the increased tolerance to G-loads, judging from the results of the second series

of experiments, did not exceed two weeks, which agrees well enough with our data, obtained in the experiments with adaptation under conditions of a rarefied atmosphere [10].

The addition of carbon dioxide to the gas mixture, depleted of oxygen (third series of experiments) was not substantially manifested in the character of the effect of the "pure" forms of hypoxia on the tolerance of the organism to G-loads. In fact, the maximal difference in the survival between the experimental and the control groups in the second series was 48.5, and in the third, 44.6%.

Adaptation to the gas environment with normal partial O_2 pressure and an elevated CO_2 content exerted no distinct influence on the tolerance to the G-loads. These data contradict the results of the investigations carried out by V. P. Zagryadskiy and Z. K. Sulimo-Samuyllo, according to whom the tolerance to G-loads after prolonged breathing of air with an elevated partial CO_2 pressure is significantly lowered [16].

The nonagreement of the results of our investigations and the data of V. P. Zagryadskiy and his associates is explained obviously by the different conditions of carrying out the experiments with CO_2, by the different criteria of evaluating the tolerance to G-loads and by the use of different types of animals. It is interesting that with an increase in the O_2 content in the gaseous environment (with the same percent of CO_2, 3-5) as these authors note (T. N. Zheludkova, V. P. Zagryadskiy et al) the tolerance to G-loads of rabbits, according to the data on changes in breathing, pulse, EKG and EEG, varied very little in comparison with the control experiments [16].

It is quite interesting that an identical increase in the tolerance to G-loads in the mice of the second and third series occured with different characteristics of the red blood. In fact, in the mice of the second series the number of erythrocytes, reticulocytes and the amount of hemoglobin increased significantly, and in the animals of the third series these characteristics did not vary. These data permit us to assume that the overall resistance of the animals adapted to a changed gas environment is determined not so much by the oxygen capacity of the blood, as by other factors, among which an important role played by the state of the /120
function of the cardiovascular system, breathing and the tissue mechanisms [3-5, 41].

The reactions of the blood, as is obvious from the above data, in the first and second series of experiments were characterized by the stimulation of hemopoiesis; here in the experiments on the white mice with adaptation to hypoxia the increase in erythrocytes and reticulocytes was greater than with adaptation to hypercapnia. The amount of hemoglobin in the first series of experiments not only was not increased as in the second series but a tendency to

decrease was observed. Less distinct and irregular changes in the hemoglobin in dogs exposed for 4 weeks to a gaseous environment containing 1.5 - 5.0% CO_2 were observed by Miller and Dallwig et al [37, 39]. The mechanism of erythrocytosis during hypercapnia has still not been studied, and this reaction is still not completely understood biologically.

It is known that breathing mixtures of gases with an increased CO_2 content is accompanied by an suppression of the tissue respiration and a lowering of the metabolism of the organism as a whole. In breathing air with a 5.6% content of carbon dioxide, the oxygen requirement of man is lowered almost by 20%. What then is the stimulus under these conditions for activation of the hemopoietic function of the brain? A. Miller's opinion that the activity of the brain is excited by approaching tissue hypoxia as a result of suppression of the oxidation processes can be assumed only as a probable, but experimentally unconfirmed, hypothesis. Moreover, in the opinion of I. S. Repin, with breathing of a gas mixture having an increased CO_2 content the tissues of the organism do not undergo any oxygen deficiency since they convert to a lower level of metabolism and functional activity.

The results which we obtained in the third series of experiments with the complex effect of oxygen deficiency and carbon dioxide excess are not fully understandable since there not only was no activation of hemopoiesis but on the contrary a certain slow down was even noted judging from the changes in the reticulocytes. It is possible that the lack of hemopoietic reaction in subsequent series was due to the favorable effect of CO_2 on breathing, blood circulation and oxygen pressure in the blood and tissues. Thus, according to the data of Ye. A. Kovalenko [20] the addition of 5% CO_2 to a gas mixture with depleted O_2 (10%) increased the O_2 pressure in the venous blood from 37 $\pm$ 3.1 to 52 $\pm$ 2.3, in the mediocapillary blood of the brain from 47 $\pm$ 2.9 to 58 $\pm$ 1.6 and in the entire organism from 46 $\pm$ 2.5 to 49 $\pm$ 2.7 mm Hg. i.e., these characteristics approached the normal values. The direction of change in the reticulocytes permits us to assume that the reaction of the hormonal system to the stress effect of the gas environment had an adequate adaptive character.

In conclusion it should be mentioned that for an ultimate solution of the problems it will be necessary to carry out special experimental investigations.

CONCLUSIONS

1. Adaptation to hypoxia under conditions of a lowered partial oxygen pressure increases the tolerance of animals to the effect of transversely directed G-loads. /121

2. The addition of carbon dioxide to an O_2-depleted gas mixture exerts no substantial influence on the degree to which the

overall tolerance of the organism, which occurs under the influence of adaptation to hypoxia, is increased.

3. The increase in the overall tolerance of the adapted animals to the effect of G-loads has no strict correlation with the characteristics of the red blood.

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A COMPARATIVE EVALUATION OF THE EFFECTIVENESS OF DIFFERENT SCHEDULES OF ADAPTATION TO HYPOXIA

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ABSTRACT: Research was carried out on white mice and rats. Based on data from changes in the animals' weight, the number of erythrocytes, the amount of hemoglobin, oxygen requirements and survival of mice at high altitudes, we can give a comparative evaluation of the natural - high-altitude and pressure-chamber adaptations (prolonged continuous adaptation for 30 days at an altitude of 2000 and 3800 m, continuous brief adaptation for 3 days, adaptation at an altitude of 3000 - 7000 m; interrupted adaptation of daily stay at " high altitude" for 6 hours for a period of 2 weeks at "altitudes" of 3000 - 7000m). It was established that the adaptation effect, found as a result of animals remaining at high altitudes and in a pressure chamber at these same "altitudes" and with the same exposure, does not change appreciably. Under pressure-chamber conditions it makes sense to set up schedules for which the adaptation is carried out with a gradual increase in altitude up to relatively high values with a significant variation in the barometric pressure during the course of the days.

The creation of scientifically based schedules of adaptation for man and animals to conditions of lowered barometric pressure has great practical significance both for aviation and space medicine as well as for occupational and athletic physiology.

In developing such schedules it is natural that we should attempt to insure that a sufficiently high and sufficiently maintained adaptation effect be obtained for a minimally short period of time. In spite of the importance of this question it has been studied very little. All concepts concerning a schedule of carrying out adaptation to conditions of lowered barometric pressure have an empirical nature. Here, of value is the experiment on mountain climbing where certain common positions concerning a rational sceduale of adaptation were confirmed. The most widely used schedules in mountain climbing obtained were those which provide for a gradual ascent to high altitude and allow a periodic descent from it. /123

The purpose of this research was a comparative evaluation of the effectiveness of adaptation to factors of altitude which occur under natural mountain conditions and with various schedules of

pressure-chamber conditioning. To solve this problem we first of all required that we choose criteria which would permit judging as to the effectiveness of the adaptation. As we know from the literature data there is no single concept concerning this problem.

Since the center of attention of our research was a study of the possibilities and the feasibility of using adaptation to hypoxia as a means for increasing the tolerance of an organism to different extreme factors we chose as the basic sign of the effectiveness of adaptation the tolerance of animals to acute oxygen insufficiency.

In the experiments on animals we studied and compared the effectiveness of adaptation attained with continuous stay under conditions of lowered barometric pressure (mountains and pressure-chamber), with a daily residence for a period of 6 hours in a pressure chamber at "altitudes" which were gradually raised from 3500 to 7000 m (interrupted adaptation) and with continuous residence for a period of the same time at the same altitude.

METHOD

We made three series of experiments in which we used 1000 white mice and 50 white rats.

In the first series a comparative evaluation was given of the effect obtained with natural, high-altitude and continuous pressure-chamber adaptation of the animals. Here in the pressure chamber the degree of evacuation of air ("altitude") and the duration of residence in it were the same as in the mountains.

The adaptation of animals to hypoxia was carried out both at high altitude regions of Mount Elbrus at an altitude of 2000 m above sea level (Terskol) for 18 days and at an altitude of 3800 m (Ledovaya Baza) for 12 days and under pressure-chamber conditions at the same altitude and with the same exposure. In the pressure chamber in all series of experiments the humor and the carbonic acid excreted by the animals was absorbed by chemical absorbants /124
(KhPI and silica gel). Along with this the chamber was periodically ventilated as a result of which fixed conditions were maintained in it: a relative humidity of 55-85%, a temperature of 20-24°, a carbon dioxide content which did not exceed 1%. To retain these conditions service personnel entered the pressure chamber through a transfer chamber.

The control animals were chosen from the same group as the experimental animals. They were kept under conditions of the vivarium in Moscow using the same system of supply as the experimental animals.

The effectiveness and the duration of retention of adaptation to lowered barometric pressure were determined basically according to the survival of animals during ascent in the pressure chamber to

an altitude of 9000 m (rate of ascent 80-100 m/sec), with exposure in it in one series of 3-4 minutes and in the others until all of the animals died.

In the latter case the lifetime of each animal was taken into account.

From the literature data it is known that increasing the altitude promotes a more rapid development of adaptation. In this respect in the second series of experiments we determined the possibility of shortening the times of adaptation at the expense of increasing the "altitude" of ascent. Thus we investigated the possibility of obtaining a high adaptation effect for a shorter period of time.

In the second and third seried of experiments we carried out those in which the overall duration of the effect of hypoxia was shortened to 78 hours but the "altitude" was significantly increased at which the adaptation took place. In this case we studied two schedules of conditioning: a continuous gradula conditioning in the process of which the animals were placed into a pressure chamber for a period of 78 hours with a gradual increase in "altitude" and an interrupted conditioning when the total length of time in the pressure chanber was also 78 hours but the entire adaptation process was extended to 13 days. The schedule of the continuous gradual and interrupted pressure-chamber adaptations is shown on Table 1.

TABLE 1. TIME OF CONTINUOUS GRADUAL AND INTERRUPTED PRESSURE-CHAMBER ADAPTATION.

Altitude, m	Continuous, hours	Interrupted, days (6 hrs each day)	Altitude, m	Continuous, hours	Interrupted, days (6 hrs each day)
3000	6	1	5500	6	7
4000	12	2 and 3	6000	6	8
4500	6	4	6500	12	9 and 10
5000	12	5 and 6	7000	18	11 and 13

The third series of experiments was carried out for comparison /125
of the effects obtained during continuous and interrupted adaptation to altitude under pressure-chamber conditions.

With interrupted adaptation the daily residence in the pressure chamber was 6 hours $\pm$ 20 minutes.

In these series of experiments along with the tolerance of the mice to acute hypoxia for different periods of time after end of exposure we also investigated changes in the red blood of the rats.

RESULTS

In the first series of experiments it was established that the tolerance to acute oxygen starvation of mice after remaining in mountains at altitudes of 2000 to 3800 m and at the same altitudes under pressure-chamber conditions is increased almost to the same degree. In this case the adaptation effect disappears after 12-14 days following descent from "high altitude". In the animals who were apapted under natural conditions a negative phase was detected. We made our judgment concerning this on the basis that the tolerance of the experimental animals to acute hypoxia after 14 days was found to be lower than the tolerance of the control animals. After the 16-18th day in the experimental animals the altitude tolerance was again reduced and remained practically the same as in the control animals.

As was shown above for a clearer explanation of the role of "altitude" in the adaptation effect in the second series of experiments we carried out a comparative evaluation of tolerance to acute hypoxia after remaining in the mountains (maximum altitude 3800 m) and an interrupted pressure-chamber adaptation (maximum altitude 7000 m).

In the first four days after completion of the natural and the pressure-chamber adaptations the tolerance to hypoxia of both groups of mice was similar. The slight predominance of the adaptation effect in the mice placed under pressure-chamber conditions may apparently be due to the fact that they were tested in the first days following completion of adaptation whereas the animals who were in the mountains were tested somewhat later, on the fourth day following descent from high altitude (Table 2).

In the mice who were adapted to altitude under pressure-chamber conditions the increased tolerance to acute hypoxia was retained for 18-20 days.

The adaptation effect following residence in the mountains by the 14th day faded, after which the animals even attained a slightly increased tolerance to acute hypoxia.

Consequently the daily residence for 6 hours of animals in the pressure chamber with a gradual increase in altitude (for 2 weeks from 3000-7000 m) led to an increase in their tolerance to acute hypoxia. Here the adaptation effect was retained for a longer period of time than after a 30-day continuous residence in mountains or in a pressure chamber at lower altitudes (2000-3800 m).

It has already been shown that in rats the changes in red blood were studied both in the process of natural and in pressure-chamber adaptations. In animals who were at an altitude of 2000 m above sea level practically no changes were observed in the red blood The residence of rats at an altitude of 3800 m under high-altitude

TABLE 2. SURVIVAL OF MICE (IN %) AT AN ALTITUDE OF 9000 m FOR DIFFERENT PERIODS OF TIME FOLLOWING DESCENT FROM THE MOUNTAINS AND INTERRUPTED PRESSURE CHAMBER ADAPTATION. /126

Group of Animals	Time after end of adaptation, days					
	4	14	16	18	20	22
Pressure chamber, altitude 3000-7000 m	75	60	55	55	55	35
Control	5	0	0	25	30	40
P	>0.01	>0.01	>0.01	unreliable		
Mountains, altitude 2000-3800 m	85	45	35	30		
Control	35	40	55	30		
P	>0.01		unreliable			

conditions accompanied by an increase in the amount of erythrocytes on an average to one million (15%). After interrupted pressure-chamber adaptation the number of erythrocytes in the peripheral blood increased on the average to two million (30%).

Both residence in mountains and daily 6-hour conditioning of animals in the pressure chamber produced an increase in hemoglobin that was similar in value, from 14-15 to 16.5-17.5 gram %.

After residence in mountains the amount of red blood was normalized for a period of 4-7 days. After conditioning in the pressure chamber the increased amount of erythrocytes and hemoglobin was retained for a period of 7-9 days; only by the 14th day did the amount of hemoglobin and erythrocytes reach a normal level.

Thus continuous residence in a pressure chamber, simulating mountains only in the degree of evacuation of air, permitted us to obtain an adaptation effect that was near to that obtained in animals under high-altitude conditions.

With interrupted pressure-chamber adaptation when the time of action on the organism by the hypoxic factor was decreased but its force was increased the time of retention of the adaptation reactions of the red blood and the increased tolerance to acute hypoxia esceeded the time of retention of the effect following residence in mountains by almost 2 times, at the relatively low altitudes of 2000-3800 m.

Consequently, under pressure-chamber conitions, apparently /127
it makes sense to use schedules of adaptation which provide for a gradual ascent to high altitudes.

Research is known in which an adverse effect has been noted on the organism of animals from a periodic ascent in a pressure chamber

to different altitudes [1].

If we analyze the conditions of the above experiments and compare them with the results of investigations by us and by other authors who have found a positive effect, we can make the assumption that the negative results obtained by these authors are due to unsuccessful schedules of adaptation.

If we assume that the adaptation effect is determined only by the time and the force of the hypoxic factor then continuous residence of animals in a pressure chamber at the same altitudes and for the same period of time as with interrupted adaptation (see Table 1) would have to give a similar effect and shorten the total time spent in conditioning to a considerable degree (Table 3).

TABLE 3. LIFETIME OF MICE (IN MINUTES) AT HIGH ALTITUDE FOR DIFFERENT PERIODS OF TIME FOLLOWING CONTINUOUS AND INTERRUPTED RESIDENCE IN A PRESSURE CHAMBER.

Group	Time after end of adaptation, days					
	1	6	9	14	19	22
After continuous adaptation	13.3	15.2	11.1	7.1	3.3	1.9
Control	11.1	6.3	1.9	7.2	2.6	7.0
P	<0.5	>0.5	>0.01	<0.5	<0.5	<0.5
After interrupted adaptation	26.2	3.9	13.9	3.8	3.5	
Control	7.2	2.6	7	2.7	3.8	
P	>0.01	>0.01	>0.5	<0.5	<0.5	

The duration of retention of the adaptation effect following interrupted and continuous pressure-chamber adaptations was almost the same. Howe er, altitude tolerance of animals following interrupted adaptation was found to be considerably higher than the tolerance to acute hypoxia of animals who remained continuously at "high altitude" in the pressure chamber.

Just as in the previous series, changes in the tolerance of animals to acute hypoxia after interrupted adaptation had a clearly expressed wave-shaped character. The shorter period of time of retention of altitude tolerance in this series of experiments in comparison with the previous ones we are inclined to attribute to seasonal factors.

As has been shown, the increase in the number of erythrocytes /128 and the amount of hemoglobin in the animals after remaining in the pressure chamber as a rule was retained for a period of 7-9 days.

On the second day followning completion of the three-day continuous adaptation the number of erythrocytes on the average exceed- the number of erythrocytes of the control group by 400,000, by the

sixth-seventh days a considerable increase was noted in the number of erythrocytes (to 1-1.5 million) with a subsequent decrease to the original values. Changes in the amount of hemoglobin were not associated with changes in the number of erythrocytes: on the second day following completion of the adaptation the increase in hemoglobin was more significant, by the sixth day the amount of hemoglobin was decreased to the original level and then remained in this range.

In this series of experiments the blood was taken also from mice. Interrupted pressure-chamber adaptation produced a gradual significant increase in the number of erythrocytes on the average from 7,700,000 to 11,500,000 and a rapid decrease in their number after cessation of the effect of "altitude" too8,290,000 by the eighth day. Such a large increase in the number of erythrocytes was accompanied also by an increase in the amount of hemoglobin.

The dynamics of changes in the red blood in mice with continuous adaptation we e found to be to a significant degree similar to changes of red blood in the rats.

Thus in spite of the equal period of time and the strength of the effect of the hypoxic factor in these two series of experiments there are nevertheless significant distinctions both in the increased altitude tolerance obtained as a result of adaptat on and in changes in the red blood. Apparently for the process of adaptation large fluctuations in the barometric pressure throughout the days has significance.

CONCLUSIONS

1. The adaptation effects obtained as a result of residence of animals in the mountains (2000 and 3700 m) and in the pressure chamber at the same "altitudes" and for the same period of time do not differ substantially.

2. Under pressure-chamber conditions it makes sense to create schedules for which the adaptation is carried out with a gradual in crease in altitude up to relatively high values and with significant fluctuations in barometric pressure throughout the period.

3. The high effectiveness of an "interrupted" conditioning schedule in the pressure chamber gives a basis for its practical utilization both for keeping the previously attained adaptation and to produce the primary effect.

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THE EFFECT OF HYPOXIA ON THE CONDITION OF DEFENSE MECHANISMS OF THE ORGANISM OF A MOUSE

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ABSTRACT: In the experiments on mice placed continuously for a period of 2 weeks into a ventilated pressure chamber with a pressure of 596 mm Hg and then immunized by dead typhoid vaccine, it was shown that with this evacuation of the atmosphere no deviations either in the cellular or in humoral immunity was observed; the character of the immunomorphological reaction which develops in the subcutaneous tissue does not change at the site of the antigen injection and of the regional lymph nodes. With multiple 6-hour daily "ascents" of mice in the pressure chamber to an altitude of 4000 - 6500 m, which lasted for 10 days, in animals who were immunized after completion of the typhoid vaccine experiment, there was noted a decrease in the production of antibodies, a decrease in the amount of glycogen in the nerutrophils infiltrating the tissues at the site of injection of the antigen, and a decrease in the reactive changes from the side of the light centers of lymphoid follicles of the regional lymph nodes.

Study of the different sides of vital activity of an organism /129 under conditions of hypoxia is one of the major problems confronting space medicine. The occurrence of an emergency situation (for example, the temporary breakdown of oxygen-producing systems) may result in the astronaut being forced to live and work for a prolonged period of time in an atmosphere with a lowered oxygen content.

The purpose of this research was to study the condition of the cellular and the humoral immunity and also the characteristics of the immunomorphological reactions in the lymphoid organs and the subcutaneous tissue at the injection site of the anitgen in mice who were subjected to lowered atmospheric pressure. This problem is valid in that the data available in the literature concerning this situation with the exception of data pertaining to the lowered tolerance of an animal's organism to infection during hypoxia [4, 10, 12, 13, 20, 21, 22] are contradictory.

METHOD

The experiments were conducted on 230 male mice, the lines BAL B/C with a weight of approximately 20 grams. The first experimental group comprised 85 mice who remained continuously for a period of 2 weeks in a ventilated pressure chamber under an atmospheric pressure equal to 596 mm Hg (corresponding to an altitude of 2000 m). The second experimental group, also consisting of 85 animals, was composed of mice who remained daily for 6 hours for a period of 10 days in a pressure chamber in which the pressure was lowered every subsequent two days. The initial pressure in the chamber was equal to 462 mm Hg and the final pressure was 330 mm Hg (corresponding to altitudes of 4000 and 6500 m). The third group of mice (control group) consisted of 60 animals who remained at normal atmospheric pressure.

Two hours following the end of the experiment 40 mice from each group were injected with a hypodermic, 40 million microbe bodies of an alcohol typhoid vaccine were injected into the right /130 thigh. The animals died every 3 hours, one, three, four, five, seven, ten and 14 days after immunization (five mice from the group each time).

Determination of the amount of the VI antibodies in the serum of the blood of the immunized mice was carried out with the aid of the reaction of passive hemagglutination according to the method of Landy and Lamb [23] in the modification of Kraskina and Gutorova [6] using the erythrocytic VI-diagnosis.[1]

The phagocytic activity of the leukocytes of the blood and the absorptive power of the cells of the reticuloendothelial system (RES) was studied in unimmunized mice from the first and second experimental groups after one, three and five days following conclusion of the experiment (10 mice from each group for each period). The absorptive power of the RES cells was determined from the rate at which the blood was purified from the particles of the bodies that were injected internally using the method of Biozzy et al. [14], and the K index was computed (this reflects the total absorptive power of the RES cells) and the α-index (which shows the intensity of phagocytosis of the body by the RES cells of the liver and the spleen. The phagocytic activity of the leukocytes of the blood was studied according to the method of Berzin' and Blumberg [1] (we computed: the phagocytic number and the phagocytic index). As a control for this part of the research we used the indices of the absorptive power of the RES cells and the phagocytic activity of leukocytes from 20 mice of the third group.

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[1] The hemagglutination reaction was simulated in the department of immunology of the Moscow Scientific Research Institute of Epidemiology and Microbiology directed by V.I. Levenson to whom we express our deepest appreciation.

For the immunomorphological investigations in the immunized rats of all three groups we took "the subcutaneous tissue from the injection site of the antigen, a local (inguinal) lymph node and the spleen. Small parts of the tissues were placed into acetone in the cold and covered with paraffin. The series cuts were dyed with hematoxylineosin, methyl green pyronine (control with ribonuclease) and by the method of amylase control.

Determination of the intensity of the plasmocellular hyperplasia in the regional lymph nodes of the immunized rats was carried out according to the method of Mikhaylov et al. [7]. We used as the index of the intensity of plasmatization the ratio of the area occupied by the plasma cells to the area of the entire lymph node. All numerical data were subjected to statistical treatment. We computed: the arithmetic mean M, the mean error of the arithmetic mean m (for the seriological data, respectively, the geometric mean and the mean error of the geometric mean). The difference between the mean indices was considered to be reliable if the possible error was less than 0.05.

RESULTS

Immunological Data. Study of the production of VI-antibodies /131 in mice from the first and second experimental groups who were immunized with the typhoid vaccine showed that the overall nature of the curve which reflects the dynamics of the titers of the antibodies for different periods of time following immunization remains the same as in the control animals of the third group (Fig. 1). As far as the level of the antibodies is concerned in the serum of the blood of the experimental animals, in the mice of the first group of the titer of VI antibodies it was the same as in the control animals of the third group, whereas in mice of the second group a distinct lowering of the VI antibody titers was noted especially at the altitude of immunogenesis (Table 1).

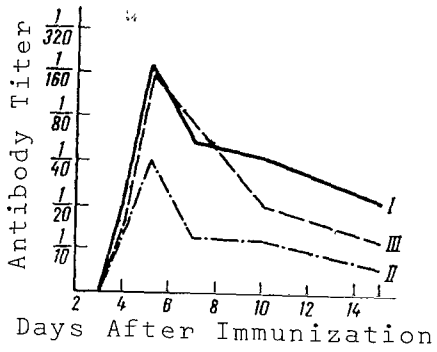

Fig. 1. Dynamics of the Titer of Antibodies in the Control and the Experimental Animals for Different Periods of Time Following Immunization. I-III. Experimental Groups.

TABLE 1. AVERAGE TITERS OF ANTIBODIES IN MICE FOR DIFFERENT PERIODS OF TIME FOLLOWING IMMUNIZATION.

Group	Times following immunization				
	4th day	5th day	7th day	10th day	14th day
I Probability of Error	22,9×0,147 >0,05	182,0×0,03 >0,05	56,2×0,15 >0,05	39,8×0,21 >0,05	22,9×0,06 >0,05
II Probability of Error	13,2×0,072 >0,05	41,3×0,12 <0,05	13,2×0,072 <0,05	12,6×0,171 >0,05	6,6×0,072 >0,05
Control	15,1×0,53	158,5×0,096	66,8×0,114	19,9×0,09	12,3×0,07

Phagocytic Activity of Leukocytes of the Blood and Absorptive Power of the RES Cells. As is obvious from the average data cited in Table 2 in unimmunized mice of the first experimental group 24 /132 hours following completion of the experiment a slight increase was noted in the absorptive power of the RES cells (index) and an increase in the number of phagocyting neutrophils of the blood (phagocytic number) whereas the phagocytic index did not change. These improvements were noted for a short period time, and after a period of three days the indices of the phagocytic activity of the blood leukocytes and the RES cells returned to normal.

Unlike the mice of the first experimental group in animals of the second group no changes were noted from the side of the absorptive power of the RES cells. At the same time the number of phagocyting neutrophils and the phagocytic index, 24 hours following completion of the experiment, were inceeased in them; however, just as in the animals of the first group these changes were short-term and even on the third day the number of phagocyting neutrophils was decreased to normal and the phagocytic index was even found to be somewhat lower than normal (Table 2).

Changes in the Subcutaneous Tissue at the Site of Antigen Injection. In the control group of mice four hours following injection of the antigen in the subcutaneous tissue an edema was observed and an expansion of the vessels with a break-up of their walls and a massive yield of neutrophils of the blood from the vessels to the surrounding tissues. After four hours at the site of the antigen injection there was a large infiltration almost entirely consisting of neutrophils in the cytoplasm of a large part of which massive glycogens were contained. On the third day a significant part of the neutrophils which infiltrated the tissue were subjected to degeneration which was preceded by the disappearance or the decrease in the amount of glycogen and cytoplasm. Apparently in the process of phagocytosis the neutrophils separated

TABLE 2. CHANGE IN THE PHAGOCYTIC ACTIVITY IN DIFFERENT GROUPS OF ANIMALS.

Day blood taken	Index	P	Phagocytic No.,%	P	Phagocytic Index	P
			First Group			
1st	0.028±0.001	<0.05	59±5.0	<0.05	5.2±0.5	>0.05
3rd	0.018±0.001	>0.05	43±6.0	>0.05	4.5±0.3	>0.05
5th	0.021±0.003	>0.05	43±7.0	>0.05	3.7±0.3	>0.05
			Second Group			
1st	0.024±0.001	>0.05	73±2.4	<0.05	10.0±0.6	<0.05
3rd	0.026±0.003	>0.05	39±2.6	>0.05	2.6±0.3	<0.05
5th	0.024±0.002	>0.05	49±4.0	>0.05	2.8±0.2	<0.05
Control	0.024±0.001		42±3.0		4.5±0.5	

the glycogen and only after the energy resources of the cells were exhausted did its degeneration occur. A large degeneration of the neutrophils is accompanied by a shart decrease in their number and a simultaneously progressive increase in the number of macrophages the number of which reached a maximum after five to seven days following injection of the antigen and then gradually decreased. The cytoplasm of the macrophages contained grains of ribonucleic acid and materials which were colored by the amylase control method (apparently glycoproteins since the coloring was not removed during preliminary treatment of the sections of amylase). On the tenth-fourteenth day in the subcutaneous tissue at the site of the antigen injection a well-expressed new formation of connective tissue was observed: proliferating non-differentiated connective elements were converted into fibroblasts which by being oriented in one direction formed nodules; there was also noted a conversion into fibroblasts of the macrophagic elements. Small congestions of mainly immature plasma cells were encountered on the seventh-tenth day following injection of the antigen around the vessel located at a slight distance from the basic source of inflammation.

Changes in the subcutaneous tissue at the site of antigen injection in the mice of the first and second experimental groups were identical to those in the control animals. One unique difference observed in the mice of the second experimental group was the decrease in the amount of glycogen in the neutrophils in the early periods of time following immunization of the animals.

Changes in the Regional (Inguinal) Lymph Nodes. In the control animals for a period of the first 24 hours after injection

of the antigen in the regional lymph nodes no changes were noted. After three days in the lymph nodes there was observed a moderately expressed desquamative catarrh of the sinuses which was not accompanied however by any significant neutrophil infiltration of the pulpy cords. In the pulpy cords of the lymph nodes there was /133
a well-expressed proliferation of reticular cells which were differentiated to the side of formation of the elements of the plasma series (plasmablast, immature plasma cells). The cytoplasm of the plasma cells contained a significant amount of ribonucleic acid.

The plasma cell hypoplasia in the cerebral rods of the lymph nodes reached a maximum development on the fourth-fifth day following immunization of the mice and then gradually decreased. The mature plasma cells began to dominate in the cerebral rods of the lymph nodes from the fifth day after injection of the antigen. Development of the plasma cell hypoplasia in the regional lymph nodes somewhat preceded the time of appearance of antibodies in the blood (well-expressed plasmatization in the lymph nodes was observed even on the third day following injection of the antigen but the antigen in the blood was first detected only on the fourth day). Simultaneously, with development of the plasma cell hypoplasia in the cerebral rods of the lymph nodes there were noted distinct changes also in the light centers of the lymphoid follicles.

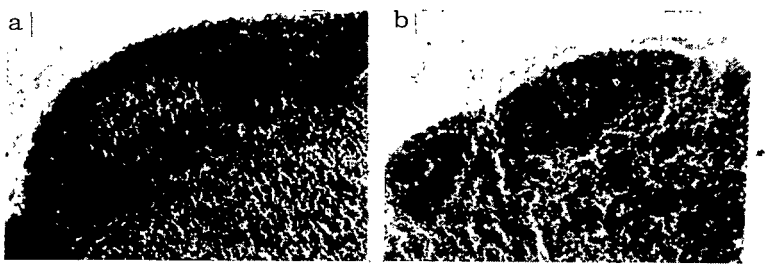

Fig. 2. a. Lymphoid Follicle with a Well-Expressed Center of Irritation in the Regional Lymph Node of the Mouse Immunized with Typhoid Vaccine; b. Hypoplasia and Absence of a Center of Irritation in the Follicle of the Regional Lymph Node of an Immunized Mouse Who Was Repeatedly Subjected to an Altitude of 4000-6500 m. /134

The latter were significantly increased in size and consisted of activated and proliferated reticular cells and blasts, the cytoplasm of which contained significant amounts of ribonucleic acid. Reactive changes in the light centers of the follicles were retained for a longer period of time than the plasma cell hypoplasia in the cerebral rods.

The overall character and the time of development of the immunomorphological changes in the regional lymph nodes of the mice from the first and second experimental groups were the same

as those in the control animals. Study of the plasma cell hypoplasia in the cerebral rods of the lymph nodes of the mice from the experimental and the control groups showed that its intensity in the animals of all the groups are the same (any difference between the average indices in the mice from the different groups is statistically unreliable). Unlike the mice in the first experimental group in which the dimensions of the light centers of the follicles of the lymph nodes were the same as in the control animals, in the mice from the second group the reactive changes from the side of the light centers were expressed more weakly and the number of lymphoid follicles in the lymph nodes was less than in the mice from the control group (Fig. 2).

In the spleen of the experimental and the control mice no such changes associated with immunization appeared.

DISCUSSION

From these data it follows that the production of antibodies in mice subjected for a period of two weeks in a pressure chamber to an atmospheric pressure equal to 596 mm Hg (first group) remains normal. No such qualitative or quantitative changes are observed from the side of the immunomorphological reactions which are developed in the subcutaneous tissue at the site of injection of the antigen and of the regional lymph nodes in the experimental animals. The short-term increase in the absorptive power of the RES cells and the slight increase in the number of phagocyting neutrophils which has been noted can possibly be explained by the irritation of the physiological system of the connective tissue which occurs under the influence of moderate hypoxia. A similar stimulation of the elements of the physiological system of the connective tissues was observed by Turanov [9] in rabbits during their ascent to an altitude of 2000 m and by Kavetskiy et al. [5] in animals who were ill with an oxygen deficiency caused by disruption of the blood circulation of step. I. /135

The decrease in the intensity of development of the antibodies in mice from the second experimental group (the animals remained daily for six hours for a period of ten days in a pressure chamber and were subjected to an altitude of 4000-6500 m) apparently is due to the increase in them of the number of immature elements of the lymphocyte series in the reactive centers of the lymphoid follicles of the regional lymph nodes. Based on contemporary ideas immature cells of the lymphocyte series along with elements of the plasmacyte series also produce antibodies [24, 25, 26]. Simultaneously it follows to emphasize that the intensity of a plasma cell hypoplasia in the regional lymph nodes in animals from the second group in comparison with the control mice did not vary. On the basis of these data we may assume that with an oxygen deficiency in the inhaled air there occurs a slow-down in the process of reproduction of the cells from the lymphocytic series whereas the reporduction and the development of cells in the plasmacytic

series is not disturbed. A similar, but higher than in other cells, sensitivity of elements of the lymphocytic series to the physical factors of the effect (x-radiation), and also to the effect of hormonal compounds, has already been noted repeatedly by a number of authors [2, 15, 16, 17, 18, 19].

The data obtained which pertained to the lowering of the production of antibodies in animals who had been repeatedly subjected in a pressure chamber to altitudes of 4000-6500 m correspond well with the results of investigations of Russian authors [3, 4, 8], who observed a decrease in the intensity of the antibody formation of approximately the same degree of evacuation of the atmosphere and contradicts the data of foreign researchers [11, 27, 28] who stated the opposite. This contradiction of data has not received, at the present time, any explanation and we may only assume that the reasons for it are concerned with the differences in setting up the experiment. We assume that for explanation of the influence of hypoxia on the development of the processes of immunogenesis it is most feasible to carry out experiments on animals who are continuously subjected to lowered atmospheric pressure. This position is based on two facts: (1) with a daily ascent and descent of animals it is impossible to exclude the well-expressed "stress" reactions which may mask the real character of the reactivity of /136 the organisms; (2) during the period that these animals are subjected to normal atmospheric pressure, especially if this period significantly exceeds the time that the animals remain in the pressure chamber, these changes which occur in the immunological reactivity of the organism during hypoxia may partially be normalized.

Unlike the mice from the first group in animals from the second group no increases in the absorptive capacity of the RES cells were observed. Apparently only moderate hypoxia produces irritation of the physiological system of connective tissue whereas at higher degrees of irritation of evacuation of the atmosphere this phenomenon does not appear.

CONCLUSIONS

1. A two-week residence of mice in a pressure chamber at an atmospheric pressure equal to 596 mm Hg (corresponding to an altitude of 2000 m) does not exert any influence on the condition of the cellular and the humoral immunity and does not produce any changes in the immunomorphological reaction which develops in the subcutaneous tissue at the site of antigen injection and of the regional lymph nodes in immunized animals.

2. With the multiple exposure of mice in a pressure chamber to an altitude of 4000-6500 m (corresponding to an atmospheric pressure of 462-330 mm Hg) there is observed a decrease in the production of antibodies in the immunized animals and also the amount of glycogen in the neutrophils which infiltrate the tissues at the site of antigen injection and a decrease in the dimensions

of the reactive centers of the lymphoid follicles of the regional lymph nodes.

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THE SIGNIFICANCE OF CERTAIN CONTROL SYSTEMS IN DEVELOPING ADAPTATION TO HYPOXIA

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ABSTRACT: We studied the role of the cerebral cortex, the cerebellar cortex, the adrenal cortex and the pituitary in the process of adaptation of an organism to a moderate degree of hypoxia. It was shown that removing the cortex of one and two of the major hemispheres will lead to a significant increase in the tolerance of animals to acute hypoxia, in which case the adaptation of such animals to moderate hypoxia will exert no substantial influence on altitude tolerance.

Removal of the cerebellar cortex reduces the tolerance of animals to acute hypoxia. After adaptation of the animals to hypoxia the removal of the adrenal cortex is not accompanied by a complete disappearance of the adaptation effect- the altitude tolerance remains higher than in the intact animals.

In spite of the fact that the problem of acclimatization to /137
high altitude conditions has attracted the attention of physicians, physiologists and biologists for more than 100 years, the physiological mechanisms responsible for this process are still to a large degree unexplained.

The development of adaptation to hypoxia (the basic factor of high altitude) results in a reconstruction of the control systems of an organism at various levels. In this respect it is of definite interest to explain the significance for the formation of adaptation to hypoxia of several of the most important regulators, under normal life conditions, which determine integration of the various functional systems. The proposed research was devoted to a study of this question. We investigated the role of the cerebral cortex, the cerebellar cortex, the adrenal cortex and the pituitary in the formation of the process of adaptation to hypoxia.

The experiments were carried out on white rats in conjunction with N.A. Roshchinaya, V.K. Martens, I.D. Bogachevaya and A.V. Shchedronovaya.

In the different series of experiments we used sexually mature males and females with a weight of 100-200 grams. Adaptation of the animals to hypoxia was accomplished both under natural condi-

tions, i.e., in the Caucasus in the region of Mt. Elbrus at altitudes of 2000 and 4000 m, and 3000-5500 m with continuous residence of the animals at these altitudes for a period of 20-30 days; we also carried out an interrupted "adaptation" in which the animals /138 remained daily for a period of 6 hours with continuously increasing altitudes from 3500-7000 m.

In the experimental animals, in the process of adaptation and at the end, we determined the amount of hemoglobin, erythrocytes and reticulocytes in the peripheral blood, we measured according to the Kalabukhov method the oxygen requirement and established by gradual ascent in a pressure chamber the altitude ceiling, i.e., the tolerance to acute hypoxia.

A relatively small amount of research has been devoted to studying the role of the cerebral cortex in the process of adaptation to hypoxia. Arkhangel'skaya noted that the removal in white rats of parts of the cortex results in a slight increase in tolerance to acute hypoxia [1], A.G. Filatova after complete removal of the cortex in pigeons also noted a small increase in tolerance [8]. Thus in these research projects it was shown that the removal from the animals of such an important regulator as the cortex does not result in a lowering of tolerance to hypoxia but unexpectedly even promotes an increase in tolerance of the organism to the effect of acute oxygen deficiency.

We were first of all interested as to whether or not the animals who had the cortex removed in the process of altitude conditioning had an increased tolerance to acute hypoxia; in the literature we have been unable to find any data on this question.

We removed one and two of the hemispheres in 45 animals. Twelve mice with one hemisphere removed, 12 with completely removed hemispheres and 10 intact animals were subjected to adaptation to hypoxia in a pressure chamber at altitudes up to 7000 m. The remaining animals who were operated on and 10 intact animals were kept for control

In the animals who were operated on and in the intact animals the residence under conditions of lowered pressure led to an increase in the blood in the number of erythrocytes, reticulocytes and hemoglobin. Earlier similar results were obtained in the laboratory by Lauer, Kolchinkaya and Turanov in experiments on dogs.

Unlike the intact animals in the rats with one and two hemispheres removed in the process of adaptation no lag in the weight of the body was noted in comparison with the control animals.

A stay at high altitude did not produce in the intact animals any changes in the amount of oxygen requirement.

In the animals who had their cortex removed, after remaining

TABLE 1. TIME OF SURVIVAL OF DIFFERENT GROUPS OF EXPERIMENTAL ANIMALS UNDER CONDITIONS OF ACUTE HYPOXIA

Group	Experimental Animals											$\bar{x}$	σ	m
	1	2	3	4	5	6	7	8	9	10	11			
Intact	3'15"	11'30"	14'	9'	17'	19'20"	16'20"	7'50"	10'40"	11'30"		11'25"	4'9"	1'6"
Intact, Acclimatized	12'45"	16'30"	16'45"	19'30"	22'	24'	21'40"	25'40"	17'30"	9'50"		18'37"	6'2"	2'06"
Without One Hemisphere	5'10"	13'20"	19'	17'20"	17'20"	16'05"	18'20"	20'20"	22'			16'35"	5'1"	1'82"
Without One Hemisphere, Acclimatized	17'	19'55"	19'	18'30"	19'30"	18'	19'	21'	21'	23'	20'30"	19'40"	1'53"	0'49"
Without Two Hemispheres	11'15"	14'30"	14'30"	17'	20'	17'30"	18'30"	24'30"	19'10"	15'20"		17'15"	3'63"	1'21"
Without Two Hemispheres, Acclimatized	12'20"	20'	18'30"	18'30"	25'30"	20'20"	20'10"	25'	26'	20'		20'39"	3'74"	1'24"

TABLE 2. TIME OF SURVIVAL OF DIFFERENT GROUPS OF EXPERIMENTAL ANIMALS UNDER CONDITIONS OF ACUTE HYPOXIA

Group	Experimental Animals										$\bar{x}$	σ	m
	1	2	3	4	5	6	7	8	9	10			
Acclimatized Without Cerebellar Cortex	10'	8'30"	3'20"	12'	14'	5'	11'40"	15'10"			9'57'	3'8"	1'42"
Control Without Cerebellar Cortex	2'20"	15'10"	15'	3'15"	2'10"	5'40"	1'30"	3'05"	2'20"		5'40"	5'27"	1'9"
Acclimatized, Intact	5'45"	3'45"	15'10"	15"	12'	19'10"	7'10"	7'30"	15'20"	10'50"	11'10"	6'18"	2'6"
Control, Intact	10'45"	10'	8'40"	10'50"	15'	7'50"	3'05"	1'20"	14'	2'30"	8'21"	4'76"	1'58"

in a pressure chamber there was noted an insignificant statistically unreliable decrease in the oxygen requirement.

Removal of one and especially of two of the hemispheres led to a significant increase in the tolerance of the animals to acute hypoxia (Table 1). Adaptation of the animals who had their cortex removed to conditions of lowered barometric pressure increases the /140 altitude ceiling relatively insignificantly. However, it nevertheless remains somewhat higher than in the intact animals who were adapted to the same conditions.

Thus in animals after the removal of the cerebral cortex the tolerance of the respiration center to acute hypoxia is significantly increased.

Adaptation of the animals who had the cortex removed to conditions of lowered barometric pressure leads to a further increase in the resistance of the respiration center to hypoxia. In this case removal of one hemisphere produces almost the same increase in resistance of the animals to hypoxia as does the removal of two hemispheres.

Adaptation of the animals with cortex removed leads to a further slight increase in the tolerance of the respiration center to hypoxia. This effect is expressed considerably less than the effect which is caused only by the operational removal of the cortex.

The role of the cerebellar cortex in the process of adaptation of an organism to hypoxia has not been studied sufficiently. There exist only data concerning injury of the cerebellar cortex, its partial removal in puppies and in rats leads to a decrease in altitude tolerance [2].

To explain the role of the cerebellar cortex in the process of adaptation of animals to acute and to chronic oxygen deficiency we carried out experiments in which the cerebellar cortex was removed from the animals after which they were subjected to the effect of lowered barometric pressure. The experimental results showed that after removal of the cerebellar cortex (morphological control permitted establishing that in more than 50% of the animals it was removed completely) there was noted a decrease in the number of erythrocytes and the amount of hemoglobin in the peripheral blood and the animals lagged in weight.

The tolerance of the animals who were operated on to acute hypoxia established according to the time of retention of life of the rats at high altitudes remained lower than in the intact animals (Table 2). A prolonged stay of such animals under conditions of lowered barometric pressure was accompanied by an increase in the erythrocytes, reticulocytes and hemoglobin in the blood and an increase in the altitude ceiling. These data confirm the results of research previously carried out by Barbashovaya. Here no substantial change in the oxygen requirement was noted. The cellular

structures of the cerebellar cortex are quite sensitive to oxygen deficiency with respect to which we might assume that removal of the cerebellar cortex similar to extirpation of the cerebral cortex, may lead to an increase in the tolerance of the organism to acute hypoxia. However, such does not happen. The difference in the appearance of the adaptation effect following removal of the cerebellar cortex and the cerebral cortex apparently is due to the non-identical influence of these formations on the subcutaneous structures and in first order on the respiration center.

In many papers it has been noted that the removal of the adrenal cortex lowers the tolerance of animals to acute hypoxia. The question as to the possibility of developing adaptation to prolonged effect of lowered barometric pressure after removal of the adrenal cortex has been studied very little. In the monograph by Barbashovaya this possibility was negated [2]. /141

Study of the process of adaptation to lowered barometric pressure in animals following removal of the adrenal cortex was carried out both under high-altitude conditions and in a pressure chamber at different altitudes.

In the process of remaining in the mountains, in animals who have undergone adrenalectomy just as in those who are intact there was detected an increase in the erythrocytes, reticulocytes and hemoglobin. No changes in the oxygen requirement here were detected. After returning from the mountains the altitude ceiling in the animals who had under gone adrenalectomy were significantly higher than in the control animals.

The results of experiments carried out in the pressure chamber permitted us to note that the adaptation effect determined from the changes in the blood and the increase in tolerance to acute hypoxia in the animals who had undergone adrenalectomy just as in the intact animals depends on the conditioning schedule under conditions of lowered barometric pressure.

Here it was found that in animals who had undergone adrenalectomy the range of altitudes for which adaptation was possible is lowered. Thus the intact animals are conditioned for prolonged stay at altitudes of 5500-6000 m at which the majority of the animals who had undergone adrenalectomy died.

In a special series of experiments the adrenal cortex in animals was removed directly after adaptation of them to altitude. Setting up the experiment in this way permitted us to obtain information as to whether there does exist "recording of acclimatization" in the adrenal cortex and what significance it has for the appearance of the adaptation effect.

The results of these experiments showed that removal of the adrenal cortex somewhat lowers the adaptation effect (altitude

TABLE 3. SURVIVAL TIME OF ANIMALS UNDER CONDITIONS OF ACUTE HYPOXIA

Group	Experimental Animals												$\bar{x}$	σ	m
	1	2	3	4	5	6	7	8	9	10	11	12			
Intact	11'20"	13'10"	11'05"	4'20"	17'15"	9'20"	8'	5'40"	13'10"	3'35"	16'05"		10'18"	4'65"	1'4"
Intact Acclimatized	15'25"	17'40"	8'10"	16'55"	17'05"	11'40"	13'	13'45"	18'10"	17'			14'53"	3'16"	1'05"
Adrenalectomized	4'	18'10"	8'20"	14'30"	12'30"	13'	5'50"	6'05"	5'	12'04"	10'30"	11'50"	10'09"	4'36"	1'3"
Adrenalectomized, "Acclimatized"	9'15"	15'	11'30"	13'40"	17'30"	18'20"	12'30"	12'30"	11'30"	12'30"	10'30"		13'09"	3'6"	1'14"

ceiling and changes in blood). However, it does not completely remove it (Table 3).

Thus, analysis of the experimental data permits us to conclude that removal of the adrenal cortex does not exclude the possibility of adapting animals to conditions of moderate degrees of atmospheric evacuation. Here in animals who have undergone adrenalectomy there is noted an increase in their tolerance to acute hypoxia and it is of such a nature as in the intact animals' changes in the blood.

Study of the adaptation to conditions of lowered barometric pressure in the mountains at altitudes of 2000 and 3800 m in animals who have undergone hypophysectomy showed that removal of the pituitary leads to a drop in the level of the hemoglobin, the number of erythrocytes and reticulocytes in the peripheral blood.

However, in spite of the lack of adaptation reactions, from the side of the blood, the tolerance to acute hypoxia after remaining in the mountains in animals who have undergone hypophysectomy is increased.

This research has shown that the removal of the most important regulators of the organism by operation (cerebral cortex, cerebellar cortex, adrenal cortex, pituitary) does not excluded the possibility of adaptation of an organism to lowered barometric pressure although it changes its course.

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THE ROLE OF CERTAIN SUBCORTICAL FORMATIONS IN THE DEVELOPMENT OF ADAPTATION TO OXYGEN DEFICIENCY

N.Z. Epshteyn

ABSTRACT: In white mice before and after adaptation to chronic hypoxia, disorders occurred in the various subcortical formations of the brain. It was shown that disorders in the reticular formation of the pons with encroachment by the nucleus reticularis tegmenti both before and after adaptation promotes an increase in the survival of rats at an altitude of 12,500 m. Disorders in the brain in the region of the ventromediothalamus and of the posterior hypothalamus promotes an increase in the tolerance of animals to acute hypoxia. Disorders in the region of the anterior hypothalamus before adaptation of the animals increases their altitude tolerance and after adaptation, lowers it.

Oxygen deficiency is a factor that man must encounter under /143
the most varying conditions. At the present time, a rather large amount of material has been accumulated concerning changes in the organism caused mainly by hypoxia and hypoxemia. However, in spite of the studies which have been carried out for many years on the problem of adaptation of an organism to oxygen deficiency, at the present time there is still no unified concept on the question of the mechanisms which lie as a basis of this. Study of materials which were available in the literature result on the conclusion that adaptation to hypoxia should be studied as a part of the overall problem of compensation of the functions which are accomplished under the regulating influence of the central nervous /144
system. Mainly, in this plan, we find an almost complete lack of data on the role of the different structures of the brain in the mechanisms of development and compensation both of acute and especially of chronic oxygen deficiency.

Taking into account the importance of the reticular formation, the thalamus and the hypothalamus in the mechanisms of the brain's activity and also data on the hypothalamus as an apparatus associated with the formation of specific and non-specific reactions such as "stress", we carried out an experimental study of the role of the above regions of the brain in the adaptation of an organism to oxygen deficiency.

The work was carried out on white rats. Using a stereotaxic apparatus in the experimental rats, we electrolytically interrupted the reticular formation of the brain or the anterior hypo-

thalamus or the posterior hypothalamus and also the thalamus of the ventromedial dorsal, ventral and medial hypothalamus. In the control animals, we carried out the operation without disruption.

As a function of the series the operation was carried out prior to adaptation of the animals to chronic hypoxia or after it.

The animals were adapted in the pressure chamber by daily ascents from 4000 to 5000 m with a 7-hour exposure. The duration of adaptation consisted of 15-30 days. Part of the animals were adapted around the clock for a period of 15 days. Then the animals were tested for survival and conditions of acute hypoxia created in the pressure chamber by ascent to an "altitude" of 12,500 m. The chamber had a glass front wall which permitted us to carefully follow the behavior of the animals. The criterion of survival in all experiments was the last breath.

The control animals were intact rats who were subjected to adaptation along with the experimental animals. The choice of data from the experiments for statistical treatment was carried out on the basis of a histological control of localization of the disorder.

In the series of experiments in explaining the role of the reticular formation we obtained statistically reliable data which indicate that disruptions in the region of the reticular formation of the brain and the nuclei and the nucleus reticularis tegmenti carried out both before adaptation and after facilitates an increase in the survival of the rats at an "altitude" of 12,500 m. In those cases when the disorder was insignificant and occurred only with a change in the morphological structure of the nerve cells, the lifetime at an "altitude" of 12,500 m was approximately the same as in the control adapted rats.

It is known that with injury to the reticular formation the reaction of awakening is sharply weakened or is completely lacking. In this case probably the tonus of the cortex caused by the normally functioning reticular formation is weakened and consequently a stable functional state of the cortex is created with respect to the action of the stimuli emitted by the numerous receptors, i.e., the sensitivity of the cerebral cortex is lowered. From this point of view our data agree with the literature data in that /145 the slowing down of the cortex or its absence facilitates an increase in tolerance to oxygen deficiency. On the other hand, G. Megun concludes that the stress-stimuli stimulate the hypothalamus-hypophesis-adrenal system through the reticular formation and therefore it is quite probable by introducing a disruption into the reticular formation we can remove the stress from the system by averting its exhaustion and in the same way we can facilitate a better adaptation to chronic oxygen deficiency. In this respect the data of Hazen and Gügenar are of interest since

they indicate that the limit of tolerance to hypoxia is determined by the condition of the nervous and humoral regulator system and by all of the characteristics in the course of the exchange processes. Hence the tactics of the prophylactic intervention must be determined by arrangements which permit knowing beforehand the exhaustion first of all of the nervous regulator mechanisms and also the humoral regulator mechanisms.

Our data also agree with this concept on disorder in the region of the ventro-medial thalamus and the posterior hypothalamus. Analysis of the experimental data obtained during the disorder of the posterior hypothalamus prior to adaptation to chronic hypoxia and after reveals a tendency for increase in survival of the animals at an "altitude" of 12,500 m. With disruption in the region of the ventro-medial thalamus the lifetime of the experimental rats under the conditions of acute hypoxia is almost twice that in the control animals. In the opinion of Bremer, Morutstsi and Megun, Rossi and Tsanketi, both the posterior hypothalamus and the ventro-medial thalamus are a part of the ascending activating system and emit to the cortex tonic discharges just as the reticular formation.

Disruptions which were applied to the anterior hypothalamus with encroachment by the area hypothalamica anterior, the nucleus paraventricularis and the lateral nuclei facilitated better adaptation to hypoxia. This is also indicated by the statistically valid data on survival by experimental rats of the control group at an "altitude" of 12,500 m ($t = 3.5$). The average time of survival of the experimental rats is 17.1 minutes, that of the control animals 7.1 minutes, i.e., 2.5 times as large. According to the data of Gess, Zager, et al., it is mainly this region of the hypothalamus which has a relationship to the specific forms of exchange and also to regulation of the numerous functions of the endocrine glands which participate in the specific forms of the exchange. In this respect we may assume that disorder in the anterior hypothalamus is accompanied by substantial changes in the exchange process which in final account change the overall reaction of the organism, in particular its tolerance to acute oxygen starvation. And if we take into account that, as a result of disorder in the anterior hypothalamus, this is reduced to a change in the liberation of the ACTH for change in the secretion of the /146
adrenal glands of the corticoids and adrenalin, then apparently we can also include the sympato-adrenal system which recently has received considerable attention.

It is interesting that in the series of experiments in which the anterior hypothalamus underwent disorders after onset of adaptation the animals died under conditions of acute hypoxia earlier than the control animals; disorder in this case was localized in the anterior hypothalamus with encroachment by the supraoptic or the paraventricular nuclei and in certain instances by the preoptic medial region. The average time of survival of the

experimental rats was 4.34 minutes, and that of the control animals 7.8 minutes ($P > 0.05$). According to the data of Barbashovaya, the demodulation of the adrenal glands is not an obstacle for acclimatization to hypoxia but an adrenalectomy substantially decreases the adaptation to acute hypoxia and acclimatization does not occur. It was established that stimulation at average elevation excites secretion of the oxycorticoids.

Disorder in the anterior hypothalamus lowers the secretion of the ACTH to the effect of trauma. Since we assume that in the formation of compensation to hypoxia there is a participation of the system of hypothalamus-hypophesis-adrenal, then an intervention in the form of a disorder in the blocking separation of the ACTH, and in the same way, a disturbing intactness of the reflector apparatus, is compiled in the organism in the process of adaptation, lowers the tolerance of the organism and leads to a more rapid death in comparison with the control animals.

Disorder in the posterior part of the thalamus in the rats who were adapted to oxygen deficiency lowers the tolerance to hypoxia. The difference in lifetime between experimental animals and the control animals is statistically proven ($P > 0.01$).

Thus in the regulation of the function in the process of adaptation to hypoxia along with the cerebral cortex substantial significance is attributed to the subcutaneous formation which is indicated by the factual material obtained that permits making the following conclusion:

1. With disorder in the reticular formation in the region of the brain and the nucleus reticularis tegmenti of the anterior hypothalamus the adaptation to chronic hypoxia occurs more effectively.

2. Disorder in the reticular formation of the brain and the nucleus reticularis tegmenti of the posterior hypothalamus, the ventro-medial thalamus in animals adapted to hypoxia substantially increases their tolerance to acute hypoxia.

3. Disorder in the anterior hypothalamus and the dorsal thalamus after adaptation to hypoxia lowers the altitude tolerance of the animal.

THE EFFECT OF AMINAZINE ON THE TOLERANCE OF ANIMALS TO ACUTE OXYGEN STARVATION*

V.P. Malkin, Ye.V. Loginova

ABSTRACT: This research was carried out on white rats and white mice. Aminazine was introduced intraperitoneally at 10 mg/1 kg weight. We determined the oxygen requirement and the survival of animals during "ascent" in a pressure chamber to high altitudes. We found that aminazine in a dose of 10 mg/kg lowers the tolerance of mice and rats to acute oxygen starvation. The increased tolerance attained in the process of pressure-chamber conditioning of the animals to acute hypoxia does not fully disappear after the introduction of aminazine. Adaptation to hypoxia increases the tolerance of the animal to the effect of aminazine.

/147

* Article Not Translated.

THE ROLE OF THE ADRENAL GLANDS IN THE DEVELOPMENT OF ADAPTATION TO HYPOXIA

N.A. Roshchina

ABSTRACT: In this research we studied the problem of the significance of the adrenal gland in the process of adaptation of animals to hypoxic hypoxia. The experiments were set up on white rats. The adaptation of animals who have undergone adrenalectomy and intact animals was carried out at high altitudes and in a pressure chamber. In the rats we investigated the red blood, the weight and the altitude tolerance.

As a result, we concluded that animals with the adrenal glands removed can be adapted to conditions of the atmosphere with a lowered amount of oxygen. In this case the adaptation change in the animals who had undergone adrenalectomy are similar to the changes detected in the intact animals.

Along with the research of Cannon, Orbeli and numerous other /151 investigators, Sel'ye established that in the process of adapting an organism to different changes in the environment an essential role is played by the adrenal glands, the acceleration of the functions of which in recent years has attained significant value in the mechanism of establishing non-specific reactions of adaptations [4, 5, 8].

Among the various effects which lead to the development of functional stress, several authors have used hypoxia [2]. With a prolonged stay of animals under conditions of a rarefied atmosphere at high altitudes (4000-700 m) many investigators have noted a hypertrophy of the adrenal glands and have evaluated this reaction as being adaptable to hypoxia.

It was found that the tolerance of animals to acute oxygen starvation is lowered after removal of the adrenal glands [1,3,7, 10,13,15], the introduction of hormonal compounds of the adrenal gland (cortizone, kendall extract, etc.) on the other hand facilitates an increase in the tolerance of animals to acute hypoxia [6,9,14]. An increase in the tolerance to hypoxia was also noted with stimulation of the adrenal glands by the adrenal corticotropnic hormone ACTH [11,12].

On the basis of these data we might have assumed that the

mechanism of adaptation to the prolonged effect of oxygen deficiency must suffer essentially after removal of the adrenal glands. This question until recent times has still been insufficiently studied. We know only of the investigation of Z.I. Barbashovaya who studied /152 the development of the adaptation syndrome in animals who had undergone adrenalectomy for a prolonged (up to a month) systematic effect of oxygen deficiency. In this case Barbashovaya, in rats who had undergone adrenalectomy, did not detect any distinct growth in the hemoglobin and erythrocytes nor any increase in the altitude tolerance which is characteristic of the intact animals [1].

The purpose of this research was to study the characteristics of development of the adaptation syndrome to prolong the effect of hypoxia in animals following removal of the adrenal glands.

METHOD

The experiments were carried on white male rats with a weight of 120 - 180 g. The adrenal glands were removed by operation under anesthetic ether.

Following adrenalectomy so as to know in advance any disorders in the aqueous-saline metabolism of the animals they drank a solution which contained glucose (5%) and NaCl (1%). For the purpose of producing adaptation to hypoxia the animals, both those who were operated on and the intact ones, were subjected to a prolonged effect of lowered barometric pressure. The first series of experiments was carried out on rats who were subjected to high-altitude conditions for 14 days at an altitude of 2000 m and 14 days at an altitude of 3800 m.

In the second series the adaptation to lowered barometric pressure was carried out in a pressure chamber according to the following schedule with a daily stay at high altitude for a period of 6 hours: the first day at 3500 m; the second day at 4000 m; the third day at 4500 m; the fourth and fifth days at 5000 m; the sixth day at 5500 m; the seventh day at 6000 m; the eighth day at 6500 m; the ninth through twelfth days at 7000 m.

As control for these animals, we used rats both intact and who had undergone adrenalectomy of the same age, sex and weight but not subjected to the effect of "altitude".

In the experimental animals in the process of adaptation the hemoglobin and erythrocytes were determined in the blood and the body weight was checked.

To evaluate the degree of adaptation to hypoxia we determined the time of survival of the animals at high altitudes. For this purpose we subjected them to ascent in a pressure chamber at a rate of 70-100 m/sec to an altitude of 11 km with a rest time of 10

minutes, then at the same rate the ascent was carried out higher with a rest time of 5 minutes at each kilometer until respiration ceased.

RESULTS

In the first series of experiments in 11 rats who had been subjected to adrenalectomy, 4 days following return from high altitude we determined the weight, the number of eryt-rocytes, hemoglobin and altitude tolerance.

These data were compared with results of investigations of the same characteristics in animals from the control groups. /153

Figure 1 shows the curves which characterize the dynamics of change in weight in the rats who had been subjected to adrenalectomy and who had been adapted to high altitude and the animals of the control groups. In looking at the curves we must pay attention to the fact that the lag in weight which is clearly expressed in the intact animals who were adapted to high altitudes appears to a lesser degree in the rats who had undergone adrenalectomy and who were adapted to high altitude. In this case it is clear that the addition in weight in the adrenalectomized animals is expressed somewhat higher than in the intact animals.

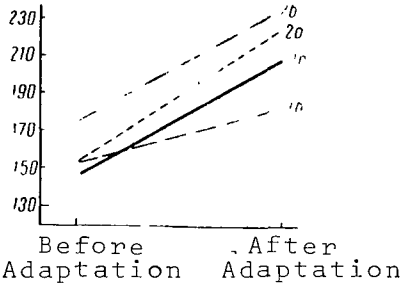

Fig. 1. Changes in Weight in Adrenalectomized (a) and Intact Animals (b) Before and After Adaptation. 1. Adapted; 2. Control Animals.

On the basis of these data we may assume that the lag in weight in animals during adaptation to conditions of lowered barometric pressure is due to a fixed degree to the change in the functional condition of the adrenal glands.

In accordance with well-known data from the literature in intact animals immediately after ascent to an altitude of 3800 m there was noted an increase in the number of erythrocytes; the amount of hemoglobin in this series of experiments during the first 10-14 days in the mountains decreased slightly and then attained values which were near to the original ones.

In the adrenalectomized animals the change in the number of erythrocytes and the amount of hemoglobin were in general similar to that cited above in the intact rat, the difference being only that the adrenalectomy produced anemia: a decrease in the number

of erythrocytes and a drop in the amount of hemoglobin. In connection with this the original background, such as the number of erythrocytes as well as the hemoglobin in the adrenalectomized animals, was lower.

It is essential that upon arrival in Moscow directly before determining the altitude tolerance, the amount of hemoglobin in the adapted adrenalectomized rats was near to the original level but the number of erythrocytes remain still at a slightly higher level. Determination in this period of the altitude ceiling showed that the adrenalectomized animals, just as the intact animals, reached a high tolerance to acute hypoxia. Table 1 cites data which characterized /154 the time of survival of animals at high altitude.

TABLE 1. LIFETIME (MIN) OF CERTAIN ANIMALS ADAPTED IN MOUNTAINS DURING ASCENT TO HIGH ALTITUDES

Group	Animals											$\bar{x}$	σ	m
	1	2	3	4	5	6	7	8	9	10	11			
AA	13	7	6	5	7	4	9	8	2	11	7	7,2	2,9	0,93
A	5	2	6	4	3	2	2	1	1	5	4	3,2	1,9	0,6
CI	7	2	3	3	8	1	3	5	9	3	5	4,5	2,5	0,8
AI						6	8	8	3	11	2	6,3	3,4	1,5

AA - Adapted Adrenalectomized Animals; A - Adrenalectomized Animals; CI - Control Intact Animals; AI - Adapted Intact Animals.

Analysis of the data given in the table shows that in animals, following the removal of the adrenaline glands the altitude tolerance is lowered slightly, however, in spite of this the adaptation of the adrenalectomized animals under high altitude conditions led to a significant increase in altitude ceiling.

The adapted adrenalectomized animals were found to be more resistant to acute hypoxia than the control animals, but in the value of the attained adaptive effect they approached the intact animals who had been adapted to conditions of high altitude.

In the second series of experiments we carried out adaptation to "altitude" in a pressure chamber of 29 adrenalectomized and 27 intact animals.

The hemotological investigation showed that the direction of changes in the number of erythrocytes in the intact and the adrenalectomized animals was similar to that we observed in the first series of experiments.

Unlike the first series of experiments after pressure chamber "adaptation" at altitudes of 7000 m in the animals there was clearly

expressed an increase in hemoglobin. Figure 2 shows changes in the amount of hemoglobin and the number of erythrocytes in the intact and the adrenalectomized animals.

In studying the curves it is obvious that in spite of the removal of the adrenal glands in the animals there is noticed a distinct increase in the number of erythrocytes and the hemoglobin, which in general is similar to the increase in the intact animals.

The dynamics of change in weight were similar to that which we described in the first series of experiments.

The second series of experiments were conducted both on animals who were stationary and those who ran freely in the chamber. /155

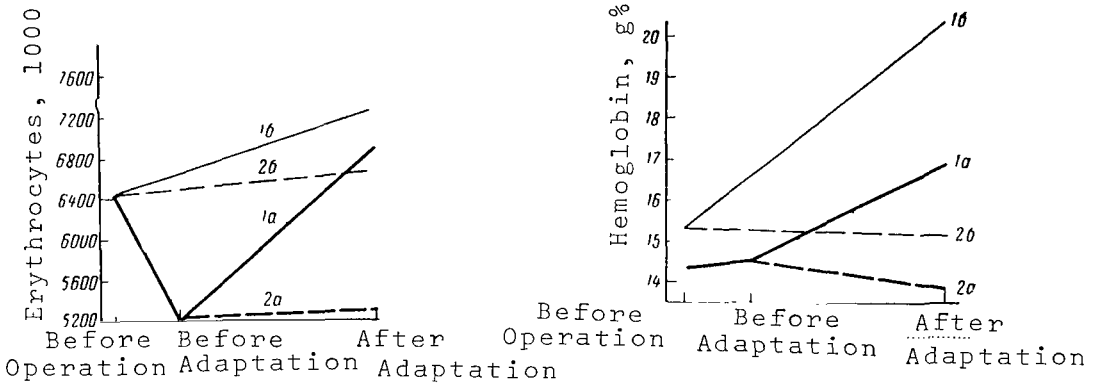

Fig. 2. Changes in the Number of Erythrocytes in Hemoglobin in the Process of the Experiment in Intact and in Adrenalectomized Animals. The Designations are the Same as in Figure 1.

Table 2 shows data which characterizes the time of survival of the stationary rats of different experimental groups, Table 3 shows analogous data obtained in experiments on animals allowed to run freely in the chamber. Including the materials from these tables, we must note that making the animals stationary itself substantially decreases the lifetime of animals at high altitudes. Somewhat expected in the experiments on the stationary animals is the longer lifetime of the adrenalectomized animals in comparison with the intact ones. This is possibly caused by the fact that making the animals strictly stationary on the bench and the introduction of electrodes determines the significance of stress-effects which determines the rapid development of the phase of exhaustion of the mechanisms of adaptation to acute hypoxia in which case the hyper-function of the adrenal glands probably plays a negative role.

The most essential result of these series of experiments is that the interrupted "adaptation" (daily stay for a period of 6 hours in a pressure chamber at altitudes from 3500-7000 m) to lowered barometric pressure of the animals who have been deprived at their

TABLE 2. LIFETIME (MIN) OF STATIONARY ANIMALS ADAPTED IN A PRESSURE CHAMBER TO HIGH ALTITUDES

Group	Experimental Animals																		$\bar{x}$	σ	m
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18			
C	5'50"	1'50"	2'50"	1'05"	47"	2'	2'	2'10"	1'15"	3'	2'30"	2'							2'16"	1,2	0,36
AI	6'	3'40"	4'40"	2'10"	2'45"	5'45"	1'50"	2'30"											3'40"	1,8	0,68
A	6'40"	2'10"	2'10"	2'20"	2'55"	5'30"	3'40"	3'30"	1'	2'50"	8'	4'	3'	3'40"	12'	6'30"	5'40"		4'30"	2,83	0,7
AA	1'20"	7'	2'55"	3'50"	4'05"	1'40"	17'15"	5'15"	3'10"	11'	10'	10'							6'27"	4,69	1,4

Designations are the same as in Table 1.

TABLE 3. LIFETIME OF ANIMALS ALLOWED TO RUN FREELY IN A PRESSURE CHAMBER DURING ASCENT TO HIGH ALTITUDES.

Group	Experimental Animals										$\bar{x}$	σ	m
	1	2	3	4	5	6	7	8	9	10			
C	6'30"	11'30"	17'20"	5'40"	5'05"	6'40"	4'	9'	11'30"	16'20"	9'19"	4,5	1,5
AI	15'40"	21'25"	17'10"	22'05"	22'40"	17'30"	21'40"	18'	19'30"	21'04"	19'40"	2,4	0,8
A	2'	7'10"	11'10"	16'05"	6'40"	8'20"	7'04"	13'20"	4'30"	10'20"	8'39"	2,7	0,9
AA	26'40"	16'40"	24'15"	22'40"	27'35"	14'10"	16'05"	16'27"	8'10"	18'15"	19'06"	6,0	2,0

Designations are the same as in Table 1.

adrenal glands led to a clearly expressed increase in their altitude tolerance and to a characteristic change in the red blood. In this case in spite of the fact that the increase in erythrocytes and hemoglobin in the adrenalectomized animals was expressed to a lesser degree than in the intact animals, the value of the adaptation effect, determined according to the average lifetime at high altitudes, in the adrenalectomized and in the intact rats was almost identical.

Analysis of the experimental results shows that removal of the /157 adrenal glands does not prevent adaptation of the animal to prolonged stay under conditions of oxygen deficiency.

In the process of adaptation in the animals without adrenal glands there appears sufficiently clearly a reaction in the red blood which is characteristic of a prolonged effect of hypoxia. In the adrenalectomized animals adapted to high altitude there was established not only the altitude tolerance to acute hypoxia but just as in the intact animals adapted to high altitude there clearly appeared adaptation reactions in respiration. In this case the value of the adaptation effect determined according to the altitude ceiling is practically the same as that established in the intact animals who were adapted to high-altitude conditions.

These data permit us to assume that the removal of such an important regulator as the adrenal cortex in animals does not exclude the possibility of developing a sufficiently high adaptation to hypoxic hypoxia.

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REACTION OF THE BLOOD TO HYPOXIA IN ADRENALECTOMIZED HYPOPHYSECTOMIZED RATS*

N.T. Blagovestova and N.A. Roshchina

ABSTRACT: In this paper we discuss changes in the blood and in the hemopoietic organs which occur in animals following removal of the adrenal glands and the pituitary and also the effect of hypoxia on the blood system.

As a result we concluded that in the adrenalectomized and the hypophysectomized rats under the operation anemia is observed. Under the influence of hypoxia in the adrenalectomized animals erythrocytosis appeared, whereas in the hypophysectomized animals no stimulation of the blood system was noticed.

/158

* Article Not Translated.

THE SIGNIFICANCE OF THE PITUITARY IN THE DEVELOPMENT OF ADAPTATION TO HYPOXIA

N. A. Roshchina

ABSTRACT: In this paper we study the role of the pituitary in the process of adaptation of rats to hypoxia. The experiments were carried out on white rats both intact and hypophysectomized. The adaptation of the animal to hypoxia was carried out in the mountains at altitudes of 2000-3800 m. In the animals we investigated the red blood, the weight and the altitude tolerance during "ascent" in a pressure chamber. The investigation showed that in the hypophysectomized animals the altitude tolerance to acute hypoxia is increased on a background of progressive anemia.

Removal of the pituitary does not essentially change the altitude tolerance of the animals who have been operated on in comparison with the intact animals.

In evaluating hypoxic hypoxia as an influence which produces /166
the development of overall functional stress it is natural to assume that the increase in activity of the pituitary has significant value for the adaptation of the organism to oxygen deficiency.

This point of view has a definite experimental basis. Thus it is known that the introduction into the animals of ACTH (adrenal corticotropic hormone) increases their tolerance to acute hypoxia [4,5].

To understand the physiological mechanism of reordering of the organism in the process of adaptation to hypoxia, it is interesting to explain the possibility of the development of adaptation by removing the "pituitary" link.

From the literature several investigations are known in which the tolerance of animals to acute hypoxia has been studied after re-/167
moval of the putiutary. The results of these papers are quite contradictory. Thus, Kou (as Kolpakov and Lauer [2] show) observed a decrease in the tolerance of the hypophysectomized animal to acute hypoxia.

In 1949 Kolpakov and Lauer noted an increase in the altitude tolerance in hypophysectomized animals after showing that following hypophysectomy during a prolonged stay of the animals under conditions of a rarefied atmosphere the adaptive reactions of the blood are lacking: an increase in the amount of hemoglobin and the number

of erythrocytes. On this basis the authors expressed the opinion that the removal of the pituitary facilitates development of adaptation of animals to conditions of prolonged stay in a gaseous environment with as low as possible oxygen pressure [2].

In 1953, Bach and Berry detected a lowered tolerance to acute hypoxia in hypophysectomized animals [7]. In 1962 Markin and Urkov did not note any substantial change in the altitude tolerance of animals in the earlier [7-10 days] periods of time following hypophysectomy [3].

In studying the tolerance of animals to the effect of the radial accelerations which produce the development of circular hypoxia Polis [6] found an increase in the survival of the hypophysectomized animal. This effect with an increase in the time following the operation of the removal of the pituitary became more clearly expressed. Thus, in the literature available to us there are contradictory data relative to the effect of removing the pituitary on the tolerance of animals to acute hypoxia and there are practically no data relative to the possibility of adaptation of hypophysectomized animal to prolonged residence under conditions of oxygen deficiency in the inhaled air.

The purpose of this paper was to study the characteristics of the development of the adaptation syndrome to prolonged effects of hypoxia in animals following removal of the pituitary.

METHOD

The experiments were carried out on white male rats with a weight of 120-180 gm. The pituitary in the animals was removed by operation based on the method developed by Bagramyan and Sakhatskaya [1][1]. Following the operation on the animals for 5-7 days they were placed in a thermostat, a large cage, where a constant temperature of +26° C was maintained. To prevent any unbalance in the aqueous-saline and the carbohydrate metabolism of the animals who were operated on, they were given a solution containing glucose (5%) and NaCl (1%).

Adaptation of the animals to lowered barometric pressure was /168
carried out in mountains where 10 hypophysectomized and 10 intact animals were placed for a period of 10 days at an altitude of 2000 m and for 14 days at an altitude of 3700 m. As a control we used the hypophysectomized and the intact animals of the same age and sex subjected to conditions of normal barometric pressure, i.e., they were not subjected to the effect of "altitude".

[1] The operation and the anatomic control were carried out by Bogachevaya.

To evaluate the adaptation effect in the experimental animals we investigated the blood (the amount of hemoglobin and the number of erythrocytes) and the body weight and determined the tolerance to acute hypoxia in the pressure chamber by means of gradual ascent.

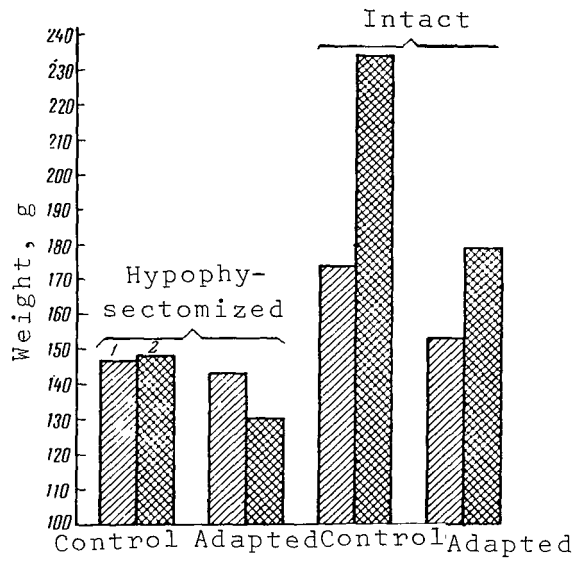

Fig. 1. The Weight of the Hypophysectomized and Intact Animals Before (1) and After (2) the Experiment (Mean Data).

RESULTS

It is known that removal of the pituitary causes a complicated restructuring of the entire endocrine apparatus and changes in the physiological condition of teh animal. Following hypophysectomy there is noted an involution of all of the glands of internal secretion and a slowing down of growth. According to these changes we can judge as to completeness of removal of the pituitary. In the experimental animals, following removal of the pituitary, in all cases there was detected a lag in the weight of the body in comparison with the control animals which on the average was 35% (see Fig. 1). Along with this the growth in the animals ceased and there was noted an involution in the glands of internal secretion. /169
Weighing the endocrine glands of the hypophysectomized animals showed a decrease in the weight of the thyroid gland on an average of 12%, the thymus 50%, the adrenal glands up to 5% and the testes up to 80%.

An anatomical control showed that in all of the animals with the exception of two the pituitary was completely removed. In these two during the post mortem we found insignificant remains of the

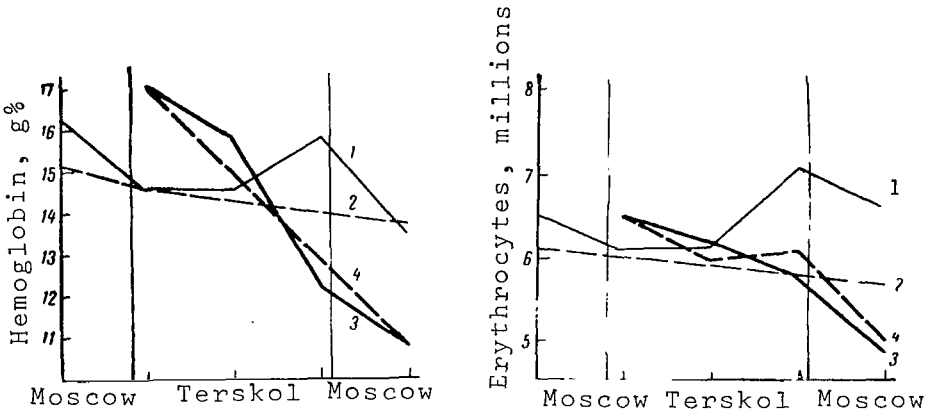

Fig. 2. Change in the amount of Hemoglobin and the Erythrocytes in the Process of the Experiment in Intact and Hypophysectomized Animals. Intact: 1. Adapted; 2. Control; Hypophysectomized: 3. Adapted; 4. Control.

posteriorpart of the pituitary. In the intact residence under high altitude conditions produced a slight lag from the control animals in increase of body weight. The body weight of the hypophysectomized animals under high-altitude conditions was also somewhat less than in the hypophysectomized control animals (Fig. 1).

In the control animals following removal of the pituitary we detected significant changes in the blood system. They appeared in the development of anemia: lowering the amount of hemoglobin and the number of erythrocytes. Analogous changes were detected also in the hypophysectomized animals subjected to conditions of high altitude (Fig. 2). Thus, residence of hypophysectomized rats under conditions of a rarefied atmosphere and altitude of 2000 and 3800 m did not prevent the development of anemia in them.

In a small series of experiments carried out under pressure-chamber conditions with daily ascents to altitudes up to 7000 m, we succeeded in four out of five of the hypophysectomized rats in detecting a slight stimulation of the heopoesis, i.e., an increase in the number of erthrocytes and the amount of hemoglobin. However, this reaction was expressed in the hypophysectomized animals to a lower degree than in the control-intact animals.

Essentially in the hypophysectomized rats, following residence in the mountains, in spite of the development of anemia we detected a distinct increase in tolerance to acute hypoxia (see the table). In the control hypophysectomized animals the altitude tolerance differed practically none from the altitude tolerance of the control intact animal. Here it should be noted only that in one animal subjected to high altitude and in one animal from the control group we detected an exceptionally long lifetime which significantly exceeds the average values. In the statistical interpretation the data obtained in the experiment with these animals were ex-

/170

LIFETIME OF INTACT AND HYPOPHYSECTOMIZED ANIMALS UNDER CONDITIONS OF ACUTE HYPOXIA (11,000 m AND ABOVE)

Group	Experimental Animals										$\bar{x}$	σ	m
	1	2	3	4	5	6	7	8	9	10			
HA	2'12"	5'	6'	3'	6'	4'	3'	6'	11'	43'	6,2	3,3	1,1
HC	5'	2'	1'5"	2'	2'	2'	1'	2'	12'	42'	3,16	1,3	0,43
C	2'	10'	2'	0,5'	2'	2'	2'	2'5"	6'	14'	3,2	2,9	1,0
CA	6'	8'	8'	3'	11'	2'	—	—	—	—	6,3	3,4	1,5

HA = Hypophysectomized, Adapted;
HC = Hypophysectomized, Control;
C = Control;
CA = Control, Adapted.

cluded. It is significant that Kolpakov and Lauer [2] in individual cases also noted in the hypophysectomized animals an extremely long lifetime at high altitude. Possibly the inclusion of data obtained on these animals also led these authors to the conclusion that removal of the pituitary increases tolerance to acute oxygen deficiency.

On the basis of analyzing the data obtained in the experiments we can make the following conclusions:

1. For 38-40 days following removal of the pituitary the tolerance of the animal to acute hypoxia does not change substantially.

2. Hypophysectomy leads to the gradual development of anemia. Residence of hypophysectomized animals at altitudes of 2000 and 3700 m in the mountains does not prevent the occurrence of anemia.

3. In hypophysectomized animals following residence under high-altitude conditions, in spite of the development of anemia, a distinct increase is noted in tolerance to acute hypoxia.

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DYNAMICA OF CHANGE IN THE OSMOTIC RESISTANCE OF ERYTHROCYTES IN HUMANS AND IN ANIMALS DURING THE PERIOD OF NATURAL ACCLIMATIZATION TO HIGH ALTITUDE

Z.I. Barbashova and G.I. Grigor'yeva

ABSTRACT: We carried out an investigation of the osmotic resistance of erythrocytes in humans and in animals in the process of adaptation to high altitudes. We studied 15 persons and 45 rats during their time of residence at an altitude of 2000-5635 m. We established that the increase in the osmotic resistance is noted in persons during active high-altitude acclimatization and correlates with the increase in the overall tolerance of the organism to acute hypoxia and G-loads. In the absence of any special physical conditioning no regular change is observed. In animals the increase in the osmotic resistance also correlates with the increase in the overall resistance of the organism. In this case we were unable to find any regularity between the changes in the osmotic resistance and the morphological composition of the blood either in persons or in the animals.

In previously published data it was shown that in the process /171
of conditioning white rats to hypoxia in a pressure chamber or to muscular activity (swimming) an increase in the osmotic resistance of the erythrocytes began. In this case the increase in the osmotic resistance of the erythrocytes occured only in those animals in which the overall resistance of the organism was high [1-3]. This caused us to make the assumption that changes in the osmotic resistance of the erythrocytes apparently may be used as one of the tests characterizing the overall state of conditioning and resistance of an organism.

In the present article we cite data on changes in the osmotic resistance of erythrocytes in humans and in white rats subjected for a period of one month to natural high-altitude conditions (in the region of Mt. Elbrus). The work was carried out in conjunction with several other laboratories, which made it possible to compare changes produced in the osmotic resistance of the erythrocytes with changes in the overall resistance of the organism determined from the reaction to acute hypoxia and the effect of the G-loads (the investigations were conducted by Malkin and Vasil'yev), and also with changes in the morphological composition of the blood (the investigations of Blagovestovaya and Roshchina).

Method

Determining the osmotic resistance of erythrocytes in humans and in rats was carried out six times: in Moscow prior to the expedition to Terskol to an altitude of 2000 m, after 8-9, 13-14 and 26-27 days of residence in the mountains at different altitudes and finally again in Moscow during the first days after return. The blood was taken from persons (from the finger) and from the rats /172
(from the caudal vein) in the amount of 0.04 mℓ of 1% solution of NaCl. 0.02 mℓ of this sample of erythrocytes were placed into a test tube with a 5 mℓ solution of NaCl of decreasing concentration. After 30 minutes the carefully mixed samples of erythrocytes were colorimetricized in a photoelectric colorimeter of SEKN-57 type with a wavelength of 536 mμ. As a control we used the sample of erythrocytes in a 1% solution of NaCl. Such a method of change yields complete agreement between the curves of hemoysis and those which were obtained after colorimetric analysis of the centrifuged transparent solutions of hemolyzed blood samples versus distilled water. Here we felt that specially constructed experiments were necessary. Simplifying the method involved the requirements of the expedition conditions.

The values obtained for the extinctions were computed in percents of the value of the extinctions for the blood samples, completely hemolyzed. Hemolysis was assumed to be completed with comparison of the densities of the samples of erythrocytes in 2-3 strongly diluted solutions of NaCl. The values of the percent of hemolysis were plotted onto graph versus the respective concentrations of NaCl. Thus we obtained curves of the nemolysis of the blood from which we constructed curves of the distribution of erythrocytes according to their resistance, similar to that described by Gitel'zon and Terskov for acid hemolysis [14]. Along the abscissa axis we plotted the given ranges of change in saline concentration in the solution and along the ordinate we plotted the percent of increase in hemolysis of the erythrocytes for each given range of saline concentration. Thus each point along the vertical corresponds to the number of erythrocytes hemolyzed in a given interval of hypotonic solution of NaCl.

A part of the persons and animals remained constantly in Terskol at an altitude of 2000 m. The others, approximately after two weeks were shifted to Ledovaya Baza to an altitude of 3900 m and remained there for a period of two weeks. They were studied only after descent to 2000 m where the laboratory was set up.

Results

Investigations on Humans. Altogether we studied 15 persons of which 10 remained constant in Terskol at an altitude of 2000 m and were involved in ordinary occupational activity (the members of the expedition varied in sex and varied quite considerably in age),

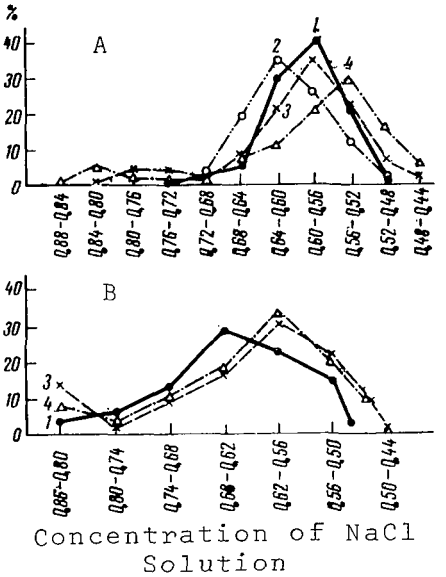
TABLE 1. HEMOLYSIS OF ERYTHROCYTES WITH DIFFERENT CONCENTRATIONS OF NaCl IN HUMANS OF THE "ALTITUDE" GROUP, %

Subject	Concentration of NaCl, %										
	0,84	0,80	0,76	0,72	0,68	0,64	0,60	0,56	0,52	0,48	0,44
Original Data in Moscow											
G.	—	—	—	0	0	5	35	70	93	100	—
M.	—	—	—	0	10	16	53	92	100	100	—
P.	—	—	—	0	0	6	40	83	97	100	—
Kh.	—	—	—	0	0	0	20	68	100	100	—
Ch.	—	—	—	0	5	9	37	77	98	100	—
$M \pm m$	—	—	—	0	3±3,3	7±3,4	37±6,8	78±5,7	98±1,7	100±0	
First Days at 2000 m											
G.	—	—	—	0	0	10	60	83	94	98	100
M.	—	—	—	0	11	40	65	86	97	100	100
P.	—	—	—	0	0	11	42	78	94	100	100
Kh.	—	—	—	0	4	22	63	85	95	99	100
Ch.	—	—	—	0	7	30	64	88	98	100	100
$M \pm m$	—	—	—	0	4±2,0	23±1,8	59±4,3	84±1,7	96±0,3	99±0,1	100±0
$P <$					0,5	0,05	0,05	Unreliable			

TABLE 1. Con'd

Subject	Concentration of NaCl, %										
	0,84	0,80	0,76	0,72	0,68	0,64	0,60	0,56	0,52	0,48	0,44
End of Residence at 3900-4200 m											
G.	—	0	3	3	4	10	34	74	94	99	100
M.	—	0	7	10	10	17	39	74	99	100	100
P.	—	0	0	3	8	12	30	58	86	96	98
Kh.	—	0	8	13	15	18	38	72	87	97	100
Ch.	—	0	4	4	8	18	41	77	94	98	100
$M \pm m$	—	0	4±1,5	7±2,1	9±1,8	15±1,7	36±2,0	71±3,4	92±2,4	98±0,2	100±0,5
$P <$			0,001	0,001	0,05	0,05	Unreliable		0,05	0,001	
In Moscow During the First Days Following Descent											
G.	0	0	6	7	8	10	11	34	75	100	100
M.	8	10	13	17	20	35	59	86	96	100	100
P.	0	0	2	5	9	19	35	59	91	98	100
Kh.	5	5	5	6	8	11	21	45	68	86	100
Ch.	4	10	12	13	14	18	22	30	70	95	100
$M \pm m$	3,4±1,5	5±2,2	8±2,1	9±2,2	11±2,4	18±3,9	29±8,2	50±1,0	80±5,7	96±2,6	100±0
$P <$			0;001	0,001	0,05	0,05	0,2	0,05	0,05	0,001	

5 persons following a 10 day residence in Terskol were gradually shifted to higher altitudes (Ledovaya Baza, 3900 m; Priyut Odinnadtsati, 4200 m) and completed ascent to the altitude of Mt. Elbrus at 5635 m. There acclimatization to high altitude from the very beginning was an active one, i.e., it involved physical labor. This was a group of males in age from 23 to 35 years. Below we shall conventionally designate this group as "altitude".



Distribution of Erythrocytes According to Osmotic Stability in Persons (A) and White Rats (B). 1. Original Values at Sea Level (Moscow); 2. First Days at an Altitude of 2000 m (Tersk 1); 3. at the End of One Month Residence at High Altitude (Terskol); 4. at an altitude of 3900 m (Ledovaya Baza). /175

Changes in the osmotic resistance of the erythrocytes were expressed most strongly in persons of the "altitude" group (Table 1.) The figure shows the distribution curves of erythrocytes based on the stability in saline solutions which vary in hypotonicity (computed from the average values in persons of the "altitude" group). In the first days of residence at an altitude of 2000 m there was noted as a rule (in 4 out of 5), a decrease in the osmotic resistance of the erythrocytes. Although the beginning and the end of hemolysis was observed with the same saline concentrations as at sea level (Moscow), i.e., at 0.72 and 0.52-0.48% respectively, but in the i - termediate saline solutions the degree of hemolysis of the erythrocytes now was higher in comparison with the original values. Thus in the range of saline concentrations from 0.60 to 0.64% on an average the amount of hemolyzed erythrocytes, as is obvious from the figure, was greater than the normal ($P<0.05$). Be the ninth day however, the values of the osmotic resistance of the erythrocytes for all saline concentrations returned to normal. At the end of residence in the mountains in persons of the "altitude" group the osmotic resistance of the erythrocytes underwent the following changes. A tendency appeared for increase in the number of the more stable

erthrocytes in the saline solution of the lowest saline concentration, (from 0.52% and below). At sea level hemolysis in two of the persons out of five ended at 0.52%, and in the other three at 0.48%, now at 0.52% the hemolysis of the erythrocytes was not ended in any of the subjects (Table 1), with 0.48% only in one, in the others only with a saline concentration of 0.44%. But simultaneously we detected a small mumber of erythrocytes on the contrary which were /176 very slightly stable, the hemolysis of which began at saline concentrations as high as 0.76%. These deviations are statistically reliable ($P<0.001$). The base of the curve of stability of the erythrocytes (see the figure) was extended; the curve had a tendency to flattening. But nevertheless the greater part of the erythrocytes in their osmotic stability did not differ strongly from the normal. Possibly this was due to the fact that determination of the osmotic resistance of the erythrocytes was carried out directly after descent from high altitude and after a very large amount of physical activity in evacuating the equipment from Ledovaya Baza. The subjects were highly fatigued and we might have expected in them certain changes in the biochemical properties of the blood which were not indifferent for the osmotic properties of the erythrocytes. It may be that these influences could counterbalance the more insignificant increase in the osmotic resistance of the erythrocytes which occured at the end of residence in the mountains and which we had determined even before the return to Moscow.

After return to Moscow and a good rest the osmotic resistance of the erythrocytes was found to be reliably different from the normal. Determinations were carried out proir to the tests of the overall tolerance to acute hypoxia and G-loads. As is obvious from the figure (A), in the blood as previously even in a still larger amount there were weakly resistant erythrocytes. Their hemolysis in three persons out of five in the "altitude" group began even with a saline concentration of 0.84%. The erythrocytes of the remaining two persons began to be hemolyzed in a solution with 0.76% (with 0.64% as the normal). However, such slightly stable erythrocytes were very few. There basic mass on the contrary possessed an increased osmotic stability. As is obvious from the figure the number of erythrocytes which hemolyze in a range of concentration from 0.60 to 0.56% is sharply decreased. The maximum of the curve is shifted significantly to the right, the number of erythrocytes which hemolyze under such low concentrations of NaCl as 0.56 - 0.44% increases significantly. Only in two persons out of the five does hemolysis cease with a saline concetnration of 0.48% and in the others this happens only at 0.44%.

The increasing osmotic resistance of the erythrocytes is in direct correlation with the increase in the overall tolerance of the organism. Prior to the expeditions into the mountains the humans of this group could barely undergo an ascent to 6000-7000 m and in this case there was observed in them gross disorders in the higher nervous activity, the EEG, the EKG and breathing (in one of

the five these disorders occurred even at 5000 m), and after a month's acclimatization in the mountains all five could remain at an al tude of 7000 m with no disruption of their functions. The tolerance to transverse G-loads was also found to be elevated (see the present collection).

Along with this the increase in the osmotic resistance of the erythrocytes in no way correlated with changes in the morphological composition of the blood. According to the data of Blagovestovaya and Roshchina, in all of the persons (although a decrease was not- /177
ed in stimulation of the hemopoiesis in the second half of residence in the mountains) in Moscow in the first days following return from the mountains the composition of the blood almost returned to the original "lowlands" value. Neither the number of erythrocytes nor the number of reticulocytes nor the composition of the hemoglobin of the blood in subjects returning from the mountains varied practically any from the normal.

Study of the osmotic resistance of the erythrocytes in the other 10 members of the expedition who differed in sex and age (from 20 years to 60) and who remained for a period of a month at an altitude of 2000 m and completed only one trip to higher altitude did not reveal any reliable deviations from the normal.

Investigations on Rats. The results obtained in investigations on 45 rats on the whole are similar to the data described for subjects of the "altitude" group. Just as in the humans of this group, and in correspondence with our previous investigations during conditioning to hypoxia in a pressure chamber, in the rats who lived for a period of 1 month on Mt. Elbrus we detected an increase in the osmotic resistance of the erythrocytes. This increase was noted also in rats who remained the entire time at an altitude of 2000 m and in rats who for the last two weeks remained at an altitude of 3900 m. Unlike changes in the osmotic resistance of the erythrocytes in persons, we found that in the rats there was no first phase of decrease on the ORE in the first days of residence in the mountains. On the contrary even of the first days there appeared a slight tendency to increase in the number of erythrocytes with increased stability as is obvious from Table 2 in which data are cited in the degree of hemolysis of erythrocytes with change in the hypotonicity of the environment and also from Figure 1 which show the curves of distribution of erythrocytes based on their osmotic stability. At the end of residence in the mountains in the first week following return to Moscow there was noted a distinct and reliable decrease in the degree of hemolysis with small concentrations of NaCl which indicates an increase in the number of erythrocytes with elevated osmotic stability. Simultaneously, just as in the humans, there appeared a slight number of osmotically very small stable erythrocytes, the hemolysis of which occurred at higher concentrations of NaCl than in the normal. The distribution curves of the erythrocytes based on their stability just as in the human were extended alon the base.

TABLE 2. HEMOLYSIS OF ERYTHROCYTES WITH VARIOUS CONCENTRATIONS OF NaCl IN WHITE RATS, %

	Concentration of NaCl Solution, %												
	0,86	0,82	0,78	0,74	0,70	0,66	0,62	0,58	0,56	0,54	0,52	0,48	0,46
Original Data in Moscow (25 Rats)													
$M \pm m$	—	0	3±0,8	9±1,9	14±1,7	30±2,4	51±2,8	72±2,4	82±1,9	88±2,1	94±1,1	100±0,1	—
First Days at 2000 m (10 Rats)													
$M \pm m$	—	—	0	1±0,2	12±0,3	27±1,6	46±2,7	67±2,6	76±2,5	85±2,2	91±1,5	99±0,3	100
$P <$				Unreliable									
At the End of Residence at 2000 m (10 Rats)													
$M \pm m$	6±2,4	11±2,8	17±3,1	22±3,7	28±4,3	36±4,2	46±3,6	62±3,1	72±3,0	81±3,1	87±2,6	95±1,6	100
$P <$			0,001	0,001	0,01	0,1	0,1	0,02	0,02	0,02	0,02	0,002	—
At the End of Residence at 3900 m (10 Rats)													
$M \pm m$	11±1,6	12±1,6	14±1,7	15±2,7	20±1,4	28±1,9	40±3,1	60±3,2	70±3,0	79±2,3	86±2,2	65±1,3	99±0,4
$P <$			0,001	0,02	0,01	0,1	0,01	0,01	0,002	0,02	0,002	0,001	
In Moscow During the First Days Following Descent (10 Rats)													
$M \pm m$	—	7±1,7	8±1,5	10±1,6	15±2,0	23±3,0	38±4,6	60±4,0	72±4,0	81±3,2	89±2,1	95±2,1	100±0
$P <$				Unreliable			0,05	0,05	0,05	0,1	0,05	0,02	0,001

It should be noted however that on the whole the increase in the ORE in the rats was expressed to a smaller degree than with experiments in conditioning to hypoxia in a pressure chamber [1, 2]. This is apparently due to the acute effect of the hypoxic stimulant. In experiments with conditioning in a pressure chamber the rats were subjected to an "altitude" of 7000 m, whereas under conditions of the described expedition the maximum altitude was 3900 m.

This increase in the ORE in the rat just as in the experiments on humans was found to be in direct correlation to the increase in the overall resistance of the organism. If the unacclimatized animals could survive at an altitude of 11,000 m for an average of 4.5 minutes, then following acclimatization to high altitude their survival was equal to 6.3 minutes, i.e., it was considerably higher (see the present collection, article by Naroshchina).

However, we could not note any distinct correlation between /179
changes in the ORE and changes in the morphological composition of the blood. Increase in the ORE at the end of residence on Mt. Elbrus still did not correlate with the increase in the hemopoesis and with counterclockwise changes in the formula of the red blood, but with return to Moscow the composition (based on the number amount of erythrocytes and reticulocytes) was practically normalized whereas the ORE remained still high.

CONCLUSION

The data obtained on changes in the ORE in the blood of healthy humans and animals acclimatized to hypoxia under natural high-altitude conditions reinforces the validity of our assumptions that determination of the ORE may be used as a test for the characteristics of the success of active conditioning in mountains accompanied by an increase in the overall resistance of the organism.

Along with this we may assume (even though the amount of material is small, it is serious in significnnce) that we can make a number of refinements in the reccomendations for using the ORE as a test for the stat of the overall conditioning of an organism. The fact is that in 10 members of the expedition we did not produce any distinct improvements in the ORE. This may be explained by the insufficiency of physical load determining the degree of which apparently is necessary in order for an altitude of 2000 m to become an effective means of raising the overall resistance of an organism/180
to changes in the ORE. But we can suggest material which shows that the correlation between the increase in overall resistance of the organism cannot always be observed. We had the possibility of determining the ORE in 4 mountain climbers who were master atheletes of high qualification, and who had been involved in mountains climbing for a period of 15 years and in recent years had made a large number of ascents. The ORE was determined in them on the 15-20th day of residence in Moscow following their return from Khan-Tengri (7000 m). Simultaneously they underwent tests of the overall re-

TABLE 3. HEMOLYSIS OF ERYTHROCYTES (in %) AT VARIOUS CONCENTRATIONS OF NaCl IN MOUNTAIN CLIMBERS 2-3 WEEKS FOLLOWING DESCENT FROM 7000 METERS

Subject	Concentration of NaCl Solution, %							
	0.76	0.72	0.68	0.64	0.60	0.56	0.52	0.48
B	0	2	4	10	19	50	100	100
S	0	0	0	5	19	62	88	100
T	0	0	2	13	25	76	100	100
Ts	0	8	8	26	54	81	94	100
M ± m	0	2±1.9	4±1.7	14±4.5	29±8.4	67±7.0	95±2.9	100±0
of the normal P <			0.5	0.25	0.5	0.25	0.5	

sistance to the effect of acute hypoxia and transverse G-loads (see the present collection). The investigation showed, as is obvious /180 from Table 3, that the ORE in the mountain climbers has no reliable deviation from the normal although the overall tolerance to acute hypoxia and G-loads was found to be significantly increased in them. Did the normalization of the ORE occur for the period of a two or three week residence at sea level, or in systematically conditioned subjects does the ORE no longer vary and is the increase in ORE in the process of conditioning characteristic only for novices? These are the questions to which we must give an answer.

It is quite possible that determining the ORE may be useful only for evaluating the positive course of the conditioning process, since the decrease in the initial period of residence in the mountains coincided with a poor state of being and the appearance of altitude illness, but the increasing ORE found in the first days following return from Mt. Elbrus to Moscow correlated with an increased tolerance of the organism.

CONCLUSIONS

1. In subjects remaining at 2000-3000 m with ascents to higher altitudes and with physical work of considerable intensity there is noted an increase in the osmotic resistance of the erythrocytes. This increase in the ORE correlates with an elevated overall tolerance of the organism which is manifested in the effect of acute hypoxia and rotation in a centrifuge and is retained after descent to sea level. No regular correlation was noted between changes in the ORE and changes in the morphological composition of the blood.

2. In persons who remain for a period of a month at an altitude of 2000 m (Terskol) and who did not undergo any special physical conditioning no regular change was noted in the osmotic resistance of the erythrocytes.

3. When white rats remained for a month at altitudes of 2000- and 3900 m this led to an increase in the osmotic resistance of the erythrocytes correlating with the increase in the overall resistance of the organism which appeared during tests in the pressure chamber with a high evacuation of atmospheric air and during rotation in a centrifuge. We were not able to find any regular correaations between the increase in ORE and changes in the morphological composition of the blood.

4. In mountain climbers of high qualification 2-3 weeks following their return from Khan-Tengri (7000 m) the osmotic resistance of the erythrocytes in no way differed from the normal which is characteristic of residents at sea level.

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CHANGE IN THE OSMOTIC RESISTANCE OF ERYTHROCYTES IN ADRENALECTOMIZED AND HYPOPHYSECTOMIZED RATS PLACED UNDER HIGH-ALTITUDE CONDITIONS*

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ABSTRACT: The investigation was carried out on adrenalectomized and hypophsectomized rats during the time of their adaptation to high altitudes at 2000 and 3900 m. It was shown that following the operation in both groups of animals there occurs an increase in the osmotic resistance of the erythrocytes. To a large degree this is expressed in the hypophysectomized rats and considerably exceeds the level of the ORE in the intact animals under high-altitude conditions. Residence of the adrenalectomized rats at an altitude of 2000 and 3900 m contributed nothing to the change in ORE caused by the operation. We discuss the possible mechanism of change in ORE and the role of hormones of the adrenal gland and the pituitary in this reaction.

/181

* Article Not Translated.

REPEATED EXPOSURE AT "HIGH ALTITUDE" AS A METHOD OF REVEALING LATENT TRACES OF ADAPTATION TO HYPOXIA

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ABSTRACT: This work was carried out on white mice and rats. The resulting phenomena were determined from the change in weight of the animals, the number of erythrocytes, the amount of hemoglobin, the oxygen requirements and the lifetime of the animals at high altitudes following single and repeated adaptation. The adaptation was interrupted; six hours per day for a period of 13 days at altitudes of 3000-7000 m. We found that in the animals following residence at high altitude even after normalization of the number of erythrocytes, the amount of hemoglobin and other characteristics, the latent trace reactions remain from the previous adaptation. The presence of trace reactions gives the possibility to the animal during repeated adaptation to more rapidly attain a higher tolerance to acute hypoxia. With multiple repetition of altitude conditioning, a summation of trace reactions is possible.

A prolonged effect on the organism of a lowered partial oxygen pressure in the inhaled air produces probably not only quantitive changes in the tissues of the vital systems such as respiration, blood circulation and hemopoiesis, but deeper qualitative changes as well, such as change in the curve of dissociation of the oxyhemoglobin [2,6,7] and increase in the sensitivity of the respirational center to CO_2 [8]. In the opinion of several of the investigators, an adaptative character even arises for the change in the tissue respiration [1]. Under the influence of a prolonged effective hypoxia, complex functional and morphological changes occur, in particular an increase in the number of capillaries in the brain [3,4]. /188

We assumed that the changes produced in the process of adaptation to hypoxia must leave prolonged traces in the organism, which will probably facilitate a more rapid and more effective adaptation of the organism to the conditions of hypoxia under its repeated effect.

In the event that each subsequent conditioning in the pressure chamber is carried out after the visible recovery of the studied characteristics, comparison of the value and duration of retention

of the adaptation effect acquired in the animals after single and repeated residence under conditions of a rarefied atmosphere must produce trace reactions.

In this paper we cite data on the latent traces of adaptation to hypoxia after high-altitude and pressure-chamber adaptation.

The investigation was carried out on 1300 white mice and 230 white rats.

The natural adaptation occured in the mountains at altitudes of 2000 m for 16 days and 3800 m for 14 days.

The adaptation to hypoxia in the pressure chamber occured for a period of 13 days with a constant increase in altitude according to the following schedule: the 1st day, 3000 m; 2nd - 3rd days, /189 4000 m; 4th day 4500 m; 5th - 6th days, 5000 m; 7th day, 5500 m; 8th day, 6000 m; 9th day, 6500 m; 11th - 13th days, 7000 m.

Daily residence of the animals in the pressure chamber was 6 hours $\pm$ 20 minutes. During the time the chamber was continually ventilated so that the CO_2 did not exceed 1%, the humidity 60 - 80% and the temperature 23 - 25° C.

We discontinued the interrupted adaptation because of its high effectiveness. As a control in all series of experiments we used animals of the same sex and age as those under the conditions of the vivarium in Moscow.

The value and time of the retention of the adaptation effect were determined from several characteristics: change in the red blood, the level of the altitude ceiling, the reaction of the cardiovascular and respirational systems to acute hypoxia and change in the body weight of the animals.

The blood for analysis in the mice and rats was taken from an incision at the end of the tail. The amount of hemoglobin was determined both by the Sali method and by the photocalorimetric method; the number of erythrocytes was computed in a Goryayev chamber. The altitude tolerance of the animals was determined by the method of gradual ascents in a pressure chamber to "altitudes" at which the animals died. Ten-minute rests were carried out every 1000 m for the mice beginning from 9000 m and for the rats from 11,000 m. The condition of the animals and the dynamics of their death were determined as a function of the altitude and time of residence there. In several series of experiments the tolerance to acute hypoxia was determined from the number of mice who survived at an altitude of 9000 m with exposure from 2 minutes 30 seconds to 4 minutes, and of rats who survived at altitudes of 11,000 - 12,000 m with a rest at each for 10 minutes. In a few series of the experiments for

TABLE 1. SURVIVAL (in %) OF MICE UNDER CONDITIONS OF ACUTE HYPOXIA (ALTITUDE OF 9000 m, EXPOSURE OF 4 MINUTES) FOR DIFFERENT PERIODS AFTER COMPLETION OF ADAPTATION.

GROUP	NUMBER OF ANIMALS	TIMES FOLLOWING COMPLETION OF ADAPTATION, DAYS			
		4	14	16	18
ADAPTED	40	85	45	35	30
CONTROL	20	35	40	55	30
P		> 0,01	UNRELIABLE		

recording the EKG, EEG and pneumograms with ascents in a pressure chamber, the rats were secured. /190

Residence at high altitudes produced an increase in the altitude tolerance of the mice, who remained there for a period of 10 - 12 days (Table 1).

After 16 - 18 days following completion of the adaptation the altitude ceiling in the mice was lowered and remained practically the same as in the control animals.

The increase in tolerance to acute hypoxia of the rats was expressed less distinctly and disappeared earlier (7th - 10th days). In the rats, who remained at an "altitude" of 3800 m, residence at high altitude produced an increase in the number of erythrocytes on an average by 1,200,000 and an increase in hemoglobin by 3.8 g%. After return from the mountains, the number of erythrocytes and the hemoglobin reached levels of the control animals at the end of the first week, i.e., somewhat earlier than the animals lost their increased tolerance to acute hypoxia.

Thus, from the test taken, the effect of natural adaptation fully disappeared by the 16th - 18th day. Two weeks later 200 mice and 60 rats who had previously lived in the mountains were subjected to interrupted pressure-chamber adaptation to hypoxia. Simultaneously animals who had never been subjected to high altitude were placed into the pressure chamber.

The data cited in Table 2 indicate the dynamics of changed in the tolerance to acute hypoxia of mice, first adapted to high altitude in which the pressure-chamber adaptation preceded residence at high altitudes.

TABLE 2. SURVIVAL (in %) UNDER CONDITIONS OF ACUTE HYPOXIA (ALTITUDE 9000 m, EXPOSURE 2 MINUTES 30 SECONDS) IN DIFFERENT PERIODS FOLLOWING SINGLE AND REPEATED ADAPTATION (AVERAGE VALUES).

GROUP	TIMES FOLLOWING COMPLETION OF ADAPTATION, DAYS								
	4	7	10	14	16	18	20	22	28
CONTROL	5	0	0	25	50	40	40	30	20
SINGLE ADAPTATION	75	70	65	60	55	55	55	35	--
REPEATED ADAPTATION	100	70	75	20	60	70	100	35	50

In spite of the fact that the repeated adaptation in the pressure chamber was carried out a month after return from the mountains and two weeks following complete recovery of the studied physiological characteristics, we nevertheless succeeded in showing traces of the preliminary mountain adaptation, about which we can judge first of all from the data of the altitude tolerance. In the /191
animals repeatedly subjected to high altitude we observed a well-expressed wave type character in the changes in tolerance to acute hypoxia: during the first days it exceeded the tolerance of the animals by 25% with single adaptation, by the 7th day it was equal, then again it was increased and by the 20th day exceeded the tolerance of animals with single adaptation by 45%. Up to the end of retention of the adaptation effect the altitude tolerance of the repeatedly adapted animals was higher than in the two other groups. As statistical processing showed, which was carried out by the method of comparing the two selective parts of the variants [5], the differences in tolerance to acute hypoxia of the animals adapted once and repeatedly, are reliable.

The changes in the altitude ceiling in the rats are expressed less clearly than in the mice.

The rats were divided into two groups. In the first we recorded the EKG, the EEG and the pneumogram. During the period of "ascent" in the pressure chamber they were fastened down. The second group were "elevated" while allowed to run freely. Securing the animals lowered the altitude tolerance. On the background of this lowering there appeared a higher tolerance of repeatedly adapted rats (Table 3). In animals who were allowed to run free during the time of "ascent" no differences were observed in the survival as a function of the conditions of training.

TABLE 3. LIFETIME OF SECURED RATS FOR VARIOUS TIMES FOLLOWING COMPLETION OF THE ADAPTATION (AVERAGE VALUES).

GROUP	TIMES FOLLOWING COMPLETITION OF ADAPTATION, DAYS						
	1	8	10	13	15	17	20
REPEATEDLY ADAPTED	18'	1'30"	6'	6'30"	7'30"	4'30"	4'5"
INITIALLY ADAPTED	6'	2'30"	4'20"	7'	5'	--	--
CONTROL	2'30"	3'	3'	1'	1'30"	3'	3'50"

The differences on the first day were statistically reliable ($P > 0.01$). In the other days a tendency was retained to a higher tolerance ($P < 0.5$).

In the rats, just as in the mice, we observed well-expressed wave-shaped fluctuations in the tolerance to acute hypoxia in the post-adaptation period.

In all secured animals the acute hypoxia (ascent to an altitude of 11,000 m) produced in the first moment a sharp drop in the pulse and respiration rate with a subsequent slight recovery only in the adapted animals and more often in the repeatedly adapted animals (Table 4).

Along with the changes in tolerance to acute hypoxia, in the rats we studied the changes in the red blood and the body weight. Both single and repeated adaptation were accompanied by an identical increase in the number of erythrocytes and the hemoglobin. After completion of the adaptation in the repeatedly adapted rats we observed a more rapid and uniform decrease in the number of erythrocytes and the amount of hemoglobin up to the level of the animals of the control group. /192

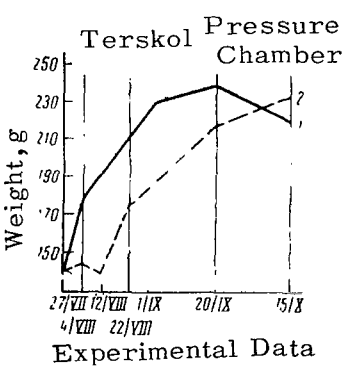

Fig. 1. Changes in Weight of Rats, Adapted to Hypoxia Singly (1) and Repeatedly (2).

TABLE 4. CHANGES IN THE PULSE AND RESPIRATION RATE DURING THE FIRST FIVE MINUTES OF THE EFFECT OF ACUTE HYPOXIA (AVERAGE DATA FOR 10 - 15 ANIMALS).

Group	"Earth"		"Altitude" - 11,000									
			1'		2'		3'		4'		5'	
	Pulse	Respiration	Pulse	Respiration	Pulse	Respiration	Pulse	Respiration	Pulse	Respiration	Pulse	Respiration
Repeatedly adapted	586	105	271	81	289	62	306	65	340	80	363	77
Singly adapted	567	108	249	85	190	70	220	70	179	53	230	50
Control	591	98	196	71	186	58	170	71	131	49	—	28
Repeatedly-Singly	<0.5		<0.5		>0.01		>0.5		>0.1		<0.5	
Repeatedly-Control	<0.5		>0.5		>0.01		>0.01		>0.01			
Singly-Control	<0.5		<0.5		>0.5		>0.01		>0.5			

We found differences also in the character of the changes in weight for the rats, repeatedly adapted (Fig. 1).

The animals first taken in the experiment in the process of pressure-chamber conditioning lost some weight. The rats of the same group in which the pressure chamber adaptation preceded residence in the mountains, not only did not lose weight, but even continued to gain. /193

Thus, after 7 - 10 days following return from the mountains in the experimental rats the number of erythroycytes, reticulocytes and the amount of hemoglobin, and after 16 - 18 days the altitude tolerance also, practically became the same as in the control

animals. In these animals however traces were retained of the previous adaptation. They facilitated a better adaptation of the organism to the repeated effect of hypoxia.

The obtained positive results of the later features of interrupted pressure-chamber adaptation for the "latent" traces of the natural high altitude served as the reason for continuation of the investigations in this direction. We were interested in the possibility of securing the trace reactions by repeated interrupted pressure-chamber adaptation. The basic condition remained that each subsequent adaptation was begun after two weeks following the visible damping of the effect of the previous one according to the reaction of the red blood and the altitude tolerance. In each "accent" along with the repeatedly adapted animals, intact animals were placed into the pressure chamber, who had been subjected prior to this time to conditions of the vivarium in Moscow.

In this series of investigations we used 750 white mice and 40 white rats.

TABLE 5. LIFETIME OF MICE AT HIGH ALTITUDE FOR DIFFERENT PERIODS FOLLOWING COMPLETION OF THE FIRST ADAPTATION (AVERAGE DATA FOR 15 ANIMALS).

Group	Times Following Completion of Adaptation, Days						
	1	7	14	21	24	27	30
Adapted	49'57"	43'11"	17'55"	39'27"	32'27"	9'29"	4'49"
Control	5'41"	10'38"	3'34"	11'37"	15'34"	17'42"	6'71"
P	0.01	0.1	0.1	0.1	0.5	UNRELIABLE	

As a result of the single interrupted pressure-chamber adaptation we obtained an effect which is retained for a period of 24 - 26 days. On the 30th day the tolerance to acute hypoxia of the adapted mice was lower than the tolerance of the control animals (Table 5).

Adaptation to hypoxia was accompanied by an increase in the number of erythrocytes on an average from 6,600,000 to 7,750,000 and an increase in the hemoglobin from 14 to 17 g%. Just as in the first series of experiments, on the 10th day of the post-adaptation /194 period the number of erythrocytes and the amount of hemoglobin de-

creased to the level of the control group.

On the first day following "descent from high altitude" in the peripheral blood the eosonophils almost completely disappeared. By the 7th - 10th day the number of eosinophils reached the original value (35 - 40/cm^3) and then continued to increase to 220 - 230 and even to 415/cm^3 by the 37th day of the post-adaptation period.

Prolonged residence in a pressure chamber produced a significant lag in weight of the rats. The average weight of this group of animals after residence at high altitude was 165 g, whereas the average weight of the control animals was 205 g. Prior to exposure of the animals in the pressure chamber the average weight of this and the other group was equal to 160 g. By the 42nd day of the post adaptation period the animals previously subjected to the pressure chamber, almost reached the weight of the control group. The weight in them by this time was increased on an average to 250 g with the mean value of the weight in the control animals being 255 g.

Thus, the periods of disappearance of the adaptation changes in the different systems of the organism were not the same. Earliest of all during the first 10 - 14 days, the amount of hemoglobin and the number of erythrocytes decreased to the original level, and then the altitude tolerance was reduced to the level of the tolerance of the control rats (24th - 26th day), after which the animals recovered the loss in weight (40th - 42nd day); the number of eosoniphils in the peripheral blood were retained the longest.

We were basically interested in the tolerance of the animals to acute hypoxia, therefore, their decrease to the level of the control group was assumed to be a criterion of damping of the adaptation effect. As shown above, by the 24th - 28th day the adaptation changes in the red blood and the increased tolerance to acute hypoxia fully disappeared. After two weeks following the lowering of the tolerance to acute hypoxia to the values of the control group and after 42 days following completion of the first exposure these same animals were subjected in the pressure chamber to adaptation to hypoxia repeatedly, according to the same schedule.

As a result of this adaptation the increased tolerance of the mice to acute hypoxia was retained for a period of 35 - 43 days both in the animals who were first exposed to "high altitude" and in those were repeatedly exposed to it (Table 6).

We were able to discern no differences in the duration of retention of increased tolerance between animals adapted one time and two times. However there are differences in the degree to which the adaptation effect was expressed. The tolerance to acute hypoxia of repeatedly adapted animals varied in a wave-shaped manner then dropped almost to the level of tolerance of the animals with single adaptation (7th, 20th days), then exceeded it by 1.5 - 2 times.

The second exposure of the animals in the pressure chamber, just as the first one, was accompanied by an increase in the number of erythrocytes and the amount of hemoglobin. In both groups the erythrocytes increased by 7000, i.e., to 1,000,000; the hemoglobin increased by 4 g%. Just as in the case when the natural high-altitude adaptation was preceded by pressure-chamber adaptation, and with a double pressure-chamber exposure the decrease in the number of erythrocytes and the amount of hemoglobin up to the level of the control group in the animals with the double adaptation occured more rapidly and more uniformly in comparison with the animals adapted only one time.

TABLE 6. LIFETIME OF MICE AT HIGH ALTITUDE FOR VARIOUS PERIODS FOLLOWING COMPLETION OF THE SECOND ADAPTATION. /195

Group*	Times Following Completion of Adaptation, Days							
	1	7	13	20	31	35	40	44
Repeatedly adapted	8'5"	4'	8'5"	2'5"	6.5"	10'0"	3'3"	3'5"
Initially adapted	5'6"	4'	4'0"	2'0"	3'7"	10'2"	3'1"	5'0"
Control	2'5"	2'	2'5"	1'6"	1'2"	4'9"	2'5"	6'9"

* Fifteen - Twenty animals in each group

In both groups of animals, residence at "high altitude" produced no drop in the number of eosinophils below the control values. However, if we take into account that in the rats after preliminary adaptation an expressed eosinophilia was retained, then the new exposure in the pressure chamber was accompanied by a significant drop in the number of esosinophils. Just as after the first adaptation, by the 7th - 8th day of the post adaptation period the number of eosinophils increased.

In this series of experiments the drop in the weight of the animals, adapted for the first time, was equal on the average to 20 g; the repeatedly adapted rats not only did not lose, but even gained weight on an average of 5 g. For this same time the control group of animals increased its weight by 45 g.

Thus, both with the combination of high-altitude and pressure-chamber and with repeated carrying out of two single type pressure-chamber adaptations we were able to show a positive effect from the previous exposures.

The third adaptat on in the pressure chamber was begun after two weeks following cessation of the effect of the previous two adaptations and after 56 days following the completion of the second adaptation.

In carrying out the first two adaptations all the test were studied only after cessation of exposure. In the third test we were interested in the dynamics of the development of the adaptation reactions in the process of hhe exposure itself in the pressure chamber. In the first two adaptations we studied the changes in the blood only in the rats, in the third we studied the dynamics of changes in the blood of the mice as well. /196

The adaptation effect after the third exposure at "high altitude" in all three groups of animals was low and had an expressed wave-shape tendency, then by completely damping it was again slightly resumed. It was retained in all for 10 - 12 days. Such variable results are apparently associated with seasonal (Spring months) variations.

No statistically reliable differences in the tolerance of the different groups of mice to the effect of acute hypoxia were detected. There was only a tendency to a higher tolerance in the animals who were exposed to high altitude for three times.

The third residence in the pressure chamber, just as the two preceding ones, produced in the rats a significant increase in the number of erythrocytes in the perpheral blood. There were several differences in the changes in the number of erythrocytes in the rats with three-time adaptation and in the animals with two-time and one-time adaptation (Fig. 2).

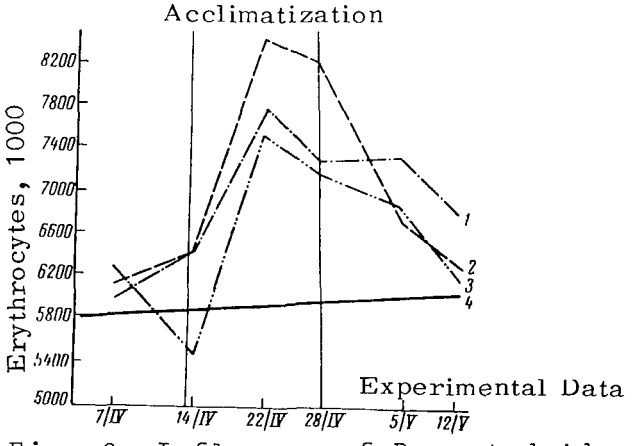

Fig. 2. Influence of Repeated Adaptations on the Number of Erythrocytes in the Peripheral Blood. 1. One-Time; 2. Two-Time; 3. Three-Time Adaptation; 4. Control.

In the first day of exposure (altitude of 3000 m) in the animals, who were adapted for the third time to hypoxia, we observed a decrease in the number of erythrocytes. In the twice adapted rats the increase in the number of erythrocytes was insignificant. In the animals first adapted to "high altitude" the increase in the number of erythrocytes was distinctly expressed. The continuation of adaptation was accompanied by an increase in the number of erythrocytes in all groups. By

the end of the exposude the greatest number of erythrocytes was in the animals who were repeatedly exposed to "high altitude" and the least in the rats who were subjected three times to altitude conditioning. After completion of the process of exposure to "high altitude" the number of erythrocytes decreased to the level of the /197
control group, first with animals with three-time adaptation and then with two-time adaptation. The animals adapted to hypoxia for the first time, retained the increased number of erythrocytes inthe peripheral blood for a longer time.

The increase in hemoglobin caused by the third exposure continued for the period of the first week of the post adaptation period. By the end of the second week the hemoglobin decreased to the original level. No differences were observed in the character of the changes in the amount of hemoglobin as a function of how many times the animal was subjected to adaptation.

In all groups of animals the oxygen requirement was regularly studied after Kalabukhov. No changes associated with adaptation were detected.

By the end of the third exposure of the animals to "high altitude" the different groups of rats had the following average weight: the group of three-time adapted rats weighed 356 g, the twice-adapted rats weighed 340 g and the singly adapted weighed 307 g. The control group of rats weighed 387 g.

Thus, as a result of the three exposures the affect of the "latent" traces of previous adaptation appeared. This was manifested in the slightly higher tolerance of the animals with three-time adaptation to acute hypoxia, on the background of the least reaction of the erythrocytes to the process of adaptation and finally in the lower lag in weight of the repeatedly adapted animals.

Summing up, we can say that in spite of the recovery of the number of physiological characteristics, in the animals after residence at "high altitude" latent trace reaction remained which may appear with repeated exposure. The trace reactions give a possibility with repeated adaptation to rapidly attain a higher tolerance to hypoxia. With repeated altitude conditioning it is possible to sum up the trace reactions. The effect of previous adaptations on the subsequent one especially clearly appear in those instances when the organism enters difficult conditions (the experiments with the animals secured).

The possibility of finding new changes on the latent traces of the previous ones is of value not only for lowering the constantly increasing tolerance of mountain climbers to the effect of acute oxygen starvation, but to facilitate the creation of more effective schedules of adaptation.

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DURATION OF THE REACTION OF THE MEDULLA OSSIUM TO ACCLIMATIZATION TO HYPOXIA

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ABSTRACT: In the high-altitude and pressure-chamber experiments we studied the duration of the hemopoietic reaction in rats under various schedules of acclimatization to hypoxia. We judged the hemopoietic condition based on the change in the rate of proliferation of the medulla osseous elements, evaluated using the statmokinetic indices and the variation curves of the amount of DNA in the cellular nuclei. The amount of DNA was studied as a sign of the intensity of the synthetic processes which are the basis of preparing the cell for division. These investigations show that prolonged single and repeated residence of animals under conditions of lowered barometric pressure, corresponding to "altitudes" of 2000-7000 m above sea level, produce a significant increase in the amount of DNA-synthesized cells and the mitotic activity of the erythroblast elements which are noted for a period of 3 - 5 weeks following cessation of the experiments. The increase in the rate of proliferation of the cells of the series did not depend on the schedule of acclimatization and was observed even in such cases when the picture of the blood which is typical for hypoxic conditions was not evolved. The mitotic activity of the myeloid cells in the experimental rats, on the contrary, was suppressed. The changes in proliferative activity of the myeloidal cells permit us to trace not only the effect of the different schedules of acclimatization but the possibility of cumulation with repeated effects of hypoxia on the organism.

Numerous investigations by Russian and foreign authors have /198
shown the possibility of a temporary increase in tolerance to hypoxic effects under the influence of the proper training, producing a given "adjustment" of the adaptation mechanisms. Among these latter apparently of no little value is the duration of the "mobilization" readiness of a system as the hemopoietic system. At the present time we can find in the literature indications that traces of such readiness in the organs of the blood system are re-

tained for a significant period of time [3,5]. Unfortunately, such information is still quite small. Moreover, it does not perfectly reflect the influence of the training schedule on the duration of retention of the trace reactions in the hemopoietic tissues. This problem is of definite theoretical and practical interest since trace reactions in the medulle ossium may have substantial value for the cumulation of adaptation changes with repeated hypoxic effects. This fact caused us to undertake a special investigation, directed mainly to finding trace reactions in the medulla ossiu, after carrying out different types of acclimatization to hypoxia. For this purpose we set up several series of experiments with prolonged single and repeated residence of animals under conditions of a lowered barometric pressure, corresponding to altitudes of 2000-7000 m. We judged the hemopoietic condition for different periods of time after acclimatization from the change in the rate of proliferation of the medulla osseous elements, which in turn were evaluated from data on determining the statmokinetic indices and in a number of instances by comparative analysis of the variation curves of the amount of DNA in the nuclei of the individual cells of the medulla ossium.

METHOD

The experiments were set up on white rats (males) weighing 130 - 170 g. All together, 124 animals were used. Of these, 58 were kept for the entire observation period under conditions of normal barometric pressure and partial oxygen pressure (Moscow). Thirty-six of the rats lived at high altitudes for one month. Of these, for the first two weeks, 17 were located at Terskol (2000 m above sea level), the next two weeks they were at Ledovaya Baza (4000 m above sea level), and 19 of the rats remained the entire time at Terskol. The other 30 rats were divided into three groups of 10 animals each. They were all subjected to acclimatization to hypoxia in a pressure chamber (Moscow). The animals of the first group were placed into a pressure chamber each day for 6 hours for a period of 2 weeks. The "altitude" on the first day was 3000 m, then it was gradually increased and on the last day was 7000 m. The rats of the second group were placed into a pressure chamber for a period of 3 days continuously. The initial "altitude" in this experiment was also 3000 m and the final, 7000 m. The third group of animals was subjected to the effect of hypoxia for 6 hours a day for a period of 2 weeks, repeatedly three times for a period of 5 months at intervals of 1 month. /199

During the experiment a dynamic observation was made of the condition of the peripheral blood in all the rats. The basic criteria in evaluating the reaction of the blood system to the effect of hypoxia was the amount of hemoglobin, the number of erythrocytes and reticulocytes.

After completion of the experiments (both high-altitude and pressure-chamber) a part of the animals were killed to study the

medulla ossium. The samples of bone marrow were taken in the following order: in animals who had remained in the mountains, 3 weeks following return to Moscow; in the animals, subjected to hypoxia in the pressure chamber, 3 weeks (first group) and 5 weeks (second and third groups) after the last effect.

The statmokinetic indices (SKI) and the amount of DNA in the cellular nuclei were determined in smears of the medulla ossium, prepared by the usual method. In the first case the smears were dyed following Romanovskiy, in the second, following Feyl'gen.

To determine the SKI (the amount of mitotic cells, blocked in the metaphase by spindle-cell toxins), we used colchicine, injected into the rats 4 hours prior to killing (0.12 mg per 100 g of body weight). The SKI were computed by separate computation of the mitoses per 100 nuclear cells of the erythroblast and myeloid series.

The amount of DNA[1] in the cellular elements of the medulla ossium was determined by the method of cytospectrophotometry. For this we used a "probe" cytospectrophotometer with photoelectric registrations of the absorption [7]. Photometric analysis of the cells was made at a wave length of 546 mμ, with an immersion objective of 90 X, photoocular 20 X, 1.3 numerical aperture and 1μ-diameter photometric scanning field. The amount of DNA in the cells was expressed weight units, picograms [8]. /200

To obtain comparable data in each sample we photometrically measured 100 cells, the nuclei of which had a circular or ellipsoidal shape.

In the medulla ossium of the rats, the erythroblast and the myeloblast elements had either a circular or ellipsoidal shape. The characteristics of the method of cytophotometry do not allow making a fine differentiation of the cells, belonging to the various shoots of the medulla ossium. Therefore, in this case we can speak only about the photometry of the "medulla osseous elements" without taking into account what type they belong to. However, this fact had no special significance for us since the problem of the investigation consisted of evaluating the proliferative ability of the medulla ossium as a whole. For this purpose it was sufficient to represent the characteristics of the DNA distribution in a given set of cells, a part of which possesses the ability of proliferate. By photometrically measuring the cells with circular and ellipsoidal nucleim we could guarantee this condition, since the cells with such nuclei in their greater part are capable of dividing [6].

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[1] To investigate the amount of DNA, we used rats who had not received colchicine.

After determining the amount of DNA in any random set of cells of the tissue under analysis and after constructing a histogram of the distribution of the amount of DNA in the individual cells, we could qualitatively characterize the condition of the proliferative processes in this tissue [1, 2, 4, 9].

RESULTS

Before we proceed to a discussion of the materials which pertain directly to the problem of this paper, let us characterize briefly the reaction of the peripheral blood in our experiments. We noted above that the basic criteria of this were the changes in the amount of hemoglobin, the erythrocytes and reticulocytes. These investigations showed that "acclimatization" to hypoxia produced changes in the red blood that are typical of the hypoxic states (increase in the amount of hemoglobin and the number of erythrocytes and reticulocytes) in the four experiments. In one experiment (Terskol) no increase in hemoglobin and erythrocytes was observed. In this case the number of eticulocytes only increased temporarily by the end of the third week residence at high altitude. After one week following return of the animals to Moscow, the number of reticulocytes dropped to the original values. The "traces" of the reaction of the red blood in the other cases were traced for a period of 1 - 2 weeks. This fact in essence determined the time of the investigations of the medulla ossium, the samples of which were taken 3 - 5 weeks following the end of the experiments. /201

From the data given in Table 1, it is obvious that in the experimental rats, regardless of the fact of whether it was high-altitude or pressure-chamber "acclimatization" to which they were subjected, the average value of the statmokinetic indices (SKI) of the erythroblast elements was found to be significantly higher than in the control group. Here we see an approximately equal degree of increase in the mitoses in the cells of a given series: literally in all cases the SKI of the erythroblasts in the experimental rate exceeded their value in the control animals by 50%. Statistical analysis confirmed the reliability of this difference. The SKI of the myeloidal cells, as is obvious from Table 1, inthe rats subjected to the high-altitude acclimatization and in the control rats, were practically the same. After the pressure-chamber effects the value of the statmikinetic indices of the myeloidal cells decreased substantially. Statistical analysis indicates that this decrease is reliable. The obtained data permit the conclusion that acclimatization to hypoxia stimulates the proliferative activity of the erythroblast elements and suppresses the myeloidal elements. Moreover, they indicate the prolonged character of this reaction, noted for a period of 3 - 5 weeks after the end of the experiments and apparently do not depend (at least in the case of the erythroblasts) on the schedule of this latter. It should also be emphasized that the changes in the proliferative activity of the medulla osseous cells observed after acclimatization are retained for a considerably longer period of time than the corresponding changes in the composition of the red blood. They appear even when

the picture of the blood which is typical of the hypoxic conditions is not evolved.

This conclusion agrees fully with the results of determining the DNA in the medulla osseous cells (Table 2). The cytophotometric investigation showed that the amount of DNA in them varies within ω range corresponding to the mitotically multiplying cells: from 6 ± 1 to 12 ± 2 ng, i.e., from a diploidal to a tetraploidal amount The values between these amounts (7.1 - 9.9 ng) may be assumed as belonging to the DNA-synthesizing cells.

Analysis of the variation curves of the amount of DNA in the individual cells of the medulla ossiom of the control rats showed that in these latter animals the number of diploidal cells is on the average 29%, the number of DNA-synthesizing cells is 33%, the number of tetraploidal cells, i.e., the cells completing the DNA synthesis and consequently prepared for future mitosis, 38%. Thus, the total amount of DNA-synthesizing cells and those having completed synthesis in these animals was 71%.

In the rats subjected to altitudes of 2000 and 4000 m, the total number of such cells after 3 weeks following return to Moscow was found to be higher, 80 and 79%, respectively. These data permit

TABLE 1. STATMOKINETIC INDICES (SKI) OF ERYTHROBLASTS AND MYELOIDAL CELLS IN THE MEDULLA OSSIUM AFTER HIGH-ALTITUDE AND PRESSURE-CHAMBER ACCLIMATIZATION. /202

Group	No. of Rats	Time of Investigation of Medulla Ossium After Experiment, weeks	SKI(M+m)	
			Erythroblasts	Myeloidal
Control	35	—	17,0±0,5	6,0±0,42
Terskol (2000m)	4	3	25,5±1,5 P<0,01	6,5±1,7 0,8>P>0,7
Terskol - Ledovaya Baza (2000-4000 m)	4	3	25,0±1,3 P<0,01	5,4±1,4 0,7>P>0,6
Pressure Chamber (3000-70000 m)				
First	10	3	24,0±1,3 P<0,01	4,4±0,17 P<0,01
Second	10	5	24,0±1,1 P<0,01	4,3±0,18 P<0,01
Third	10	5	24,3±1,2 P<0,01	3,2±0,11 P<0,01

TABLE 2. AVERAGE AMOUNT AND DISTRIBUTION OF DNA IN THE CELLS OF THE MEDULLA OSSIUM OF CONTROL AND EXPERIMENTAL RATS.

Group	Number of Animals	Total no. of Investigated Cells	Average Amount of DNA in the nucleus ng	Cells with DNA, %		
				2x (6±1), ng	2x-4x (7.1-9.9), ng	4x (12±2), ng
Control	13	1700	9.6	29	33	38
Terskol (2000 m)	8	800	10.4	20	36	44
Terskol-Ledovaya Baza (2000-4000 m)	7	700	10.1	21	36	43

the conclusion that prolonged residence of the animals in an atmosphere with a lowered amount of oxygen stimulates the synthetic processes which are the basis of preparation of the cells for dividing, and in the same manner facilitates more intense course of the processes of proliferation in the tissue being analyzed. Along with this the obtained results show that this amplification of the biosynthetic processes is retained for along period of time, being a sign of the difficult reversibility of the reaction developed in the medulla ossium. /203

CONCLUSION

Thus the group of data presented showed that residence of animals in an atmosphere with a lowered amount of oxygen was accompanied by the occurrence of definite changes from the side of the peripheral blood, which are typical for hypoxic conditions. With return to normal conditions the qualitative and quantitative composition of the peripheral blood was rapidly normalized. After 1-2 weeks the blood of the animals, subjected to acclimatization, did not differ from the blood of the control rats. However, a pronounced regeneration of the process of cellular reproductibility in the medulla ossium of the rats adapted to hypoxia was retained considerably longer (more than 3 - 5 weeks). This is indicated by the large percent of synthesizing DNA cells and those having completed synthesis, and also by the large amount of mitoses of the erythroblast series. Since no increase in the mitoses of the myloidal cells in the medulla ossium of the experimental animals was noted (the number of these latter, on the contrary, decreased), we may assume that the increase in the number of DNA-synthesizing cells and those having completed synthesis was caused by the stimulation of synthetic processes only in the erythroblast elements. No influence of the various schedules of adaptation on the rate of proliferation of the erythroblast cells was detected. In this respect it is of interest to look at the myeloidal shoots of the medulla ossium; the changes in the proliferative

activity of the myeloidal cells permit tracing not only the influence of the various schedules of acclimatization, but apparently also the possibility of cumulation of changes with the repeated effect of hypoxia on the organism.

Summing up, we can conclude that the amplification of the synthetic processes which are the basis of readying the cells for division, just as the smplification of proliferation of the cells of the erythroblast series, retained for such a long period of time after acclimatization ot hypoxia, is a sign of the difficult reversibility of the changes which occur under the effect of this factor. Analogously, the changes in the myeloidal cells must obviously be evaluated.

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THE MECHANISM OF ADAPTING WHITE MICE TO A HYPERCAPNIC GASEOUS ENVIRONMENT

V.Ye. Belay, P.B. Vasil'yev and G.D. Glod

ABSTRACT: We cite data on studying the influence of a hypercapnic gaseous environment (3 - 10% CO_2) on the functional condition of the central nervous system. The index of the reaction of the central nervous system to hypercapnia was the sensitivity of the animals to narcotics (ether, intranarcon). We established the dependence of the phase changes in the functional interrelationships of the cortex in the subsutaneous formation of the central nervous system on the degree of hypercapnia and the duration of adaptation.

Study of the mechanisms of adapting the organism to prolonged residence in a changed gaseous environment is of great practical significance in the development of systems of survival relative to the problems of aviation, astronautics, submarines, etc. Special attention must be paid to this program in studying the reaction of the organism to prolonged breathing of hypercapnic gaseous mixtures.

The character of the physiological changes, observed as a results of the effect of different degrees of hypercapnia, has been studied rather fully [1,4,6]. Here it has been established that the numerous physiological phenomena which appear with breathing of hypercapnic gas mixtures are due to the suppression of the effect of carbon dioxide on the various links of the nerve regulation [3, 5,8,12,13,15]. We must show that the literature data concerning the mechanisms of adaptation to hypercapnia are quite contradictory; this can apparently be explained by the different methodological approaches used by the authors, and also by an insufficient accounting of the time of effect of the carbon dioxide gas mixtures.

In the present paper we studied the character of the changes in the functional condition of various parts of the central nervous system of animals in the process of adaptation to various degrees of hypercapnia. As the criteria of the functional condition of the nervous system we used signs of change in the reaction of the animals to narcotic preparations. Such a methodological appraoch was found to be justified, since in studying the characteristics of the reaction of the organism to medicinal compounds under conditions of /205
a changed gas environment, we solved problems which are significant in the theoretical and practical sense [2,7,15].

METHOD

The investigations were made on 320 white male rats weighing 18 - 25 g. The intervals between the experiments on the same animals was seven days. The animals were subjected to the effect of a hypercapnic gas mixture, containing 3 - 5 or 8 - 10% carbon dioxide and an ordinary amount of oxygen. The artificial gas atmosphere was created in a special chamber with a volume of 50.4 liters, ventilated with a gas mixture from a tank. The composition of the gas mixture in the chamber was controlled with a complex gas analyzer from the firm "Godart". The reaction to the narcotics (ether and intranarcon) was studied in the control animals and in the experimental animals subjected to the effect of different degrees of hypercapnia for a period of 1 - 4 hours.

The ether narcotic was given in a hermetically sealed excicca-tor with a volume of 9.1 liters simultaneously to 10 animals (5 control and 5 experimental) for a period of 15 minutes with a concentration of ether vapors of 300 mg/liter. The intranarcon was injected intraperitoneally in a dose of 150 mg/kg (0.1 ml solution per 10 g of animal weight).

We recorded the time of onset and the total duration of the narcosis in stages III-IV after Schoen [19] and also the duration of the reverse development of narcosis after cessation of the narcotization (in the experiments with ether). The experimental material was anlyzed statistically [11] and the data of the narcotic effect of the compounds in the control and the experimental groups of animals were compared.

RESULTS

Observation of the reactions of the animals during their residence in the hypercapnic gas environment did not reveal any substantial changes in their behavior in comparison with the control animals. At the end of the first hour of breathing the hypercapnic gas mixture the animals as a rule quieted down and the notive reactions of "pursuit" disappeared. No pronounced differences were observed in the behavior of the animals as a function of the concentration of carbon dioxide in the inhaled gas mixture. However, the reaction of the mice to the pharmacological agents taken underwent changes associated both with the concentration of carbon dioxide in the gas misture and with the duration of residence of the animals in it.

Such data concerning the raaction of animals to ether for different periods of adaptation to a hypercapnic gas atmosphere are shown on Table 1. As is obvious from this material, the narcotic state in the experimental mice subjected to the effect of a gas mixture with 3 - 5% carbon dioxide content was developed approximately the same as in the control animals (from 94.2 to 109.8%). The /206
total duration of narcosis in this series of experiments (during the first 2 hours of residence in the artificial gas atmosphere)

practically did not change. However, with narcotization in the later periods toward the third hour a slight relative decrease was noted in the total duration of narcosis (84.6%), and by the fourth

TABLE 1. SEVERAL CHARACTERISTICS OF DURATION OF ETHER NARCOSIS IN WHITE MICE AFTER BREATHING HYPERCAPNIC GAS MIXTURES (AVERAGE DATA).

Sign of narcotic effect	CO_2 in gas mixture, %	Statistical Index	Time of breathing gas mixture, hour							
			1		2		3		4	
			cont.	exp.	cont.	exp.	cont.	exp.	cont.	exp.
Times of onset of narcosis from beginning of narcotization, min.	3—5	*M*.....	7.65	8.03	7.62	7.55	7.34	8.05	8.15	7.69
		% of control	—	104.8	—	99.0	—	109.8	—	94.2
	8—10	*M*.....	8.2	8.2	8.4	9.1	8.4	9.3	8.6	9.6
		% of control	—	100	—	108.2	—	110.6	—	111.5
Total duration of narcosis stages III-IV, min.	3—5	*M*.....	12.5	11.9	12.3	13.1	12.9	10.9	10.8	12.35
		% of control	—	95.5	—	106.1	—	84.6	—	113.9
	8—10	*M*.....	9.8	11.3	10.5	9.2	11.6	12.3	11.9	9.9
		% of control	—	115.4	—	87.4	—	106	—	83.3
Times of inverse development of narcosis after end of narcotization, min.	3—5	*M*.....	4.97	4.95	5.48	5.7	5.35	4.02	4.31	5.05
		% of control	—	99.8	—	104	—	75.2	—	117
	8—10	*M*.....	3.1	4.53	4.35	4.5	5.0	6.9	5.42	4.67
		%of control	—	146	—	103.2	—	138	—	86.4

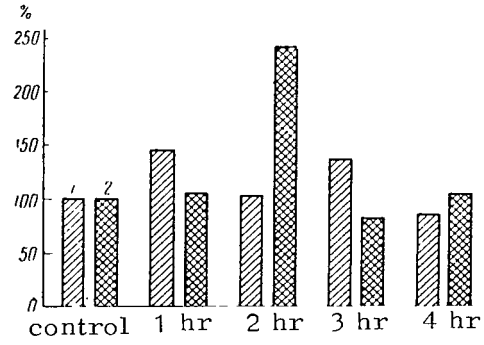
hour, an increase up to 113.9%. The time of the inverse development of narcosis after end of narcotization varied in parallel with the changes in its total duration. /207

Thus, the changes in the reaction with respect to ether in the experiments with prolonged residence of the animals in an atmosphere of 8 - 10% carbon dioxide differed in manifestation and earlier development.

Taking into account the characteristics of the pharmacological effect of ether, having primarily a cortical effect, it was interesting to compare the results obtained with the data concerning the reaction of the animals under the same methodological experimental conditions to intranarcon with the point of application primarily in the region of the subcutaneous formations of the brain. Data on the reaction of mice to intranarcon are given on Table 2.

As is obvious from the data in the table, the average duration of the intranarcon narcosis in the white mice was reliably increased ($t > 1.96$) after two hours of residence in hypercapnic gas environment, and in the other periods practically did not differ from the control data. Here the change in the reaction to the compound was expressed to a larger degree with breathing of the animals of an 8 - 10% carbon dioxide gas mixture (243%) and to a lesser degree with breathing of a 3 - 5% CO_2 mixture. /208

Based on the above positions concerning the characteristics of the effect of medicinal compounds as a function of the original functional state of the organism [9] we may assume that the narcotic effect of the compound is increased at the expense of the change in the functional mutual relationships between the cortex and the subcortex with the main development of the processes of slow down in these or other structures.



Comparative Data on Changes in the Reaction of White Mice to Narcotics Under the Influence of Prolonged Residence in a Gas Environment with 8 - 10% Carbon Dioxide Content: 1. Duration of Inverse Development of Ether Narcosis; 2. Total Duration of Intranarcon Narcosis. Average Data are in Percents of Control.

Change in the reaction to narcotics in the process of adaptation of animals to a 3 - 5% carbon dioxide gas mixture permits the assumption of a high sensitivity of the sucortical structures of the brain to the effect of carbon dioxide. In fact an increase was observed earlier in the sensitivity to the intranarcon (after two hours)

which may indicate the development of retarding processes in the subcortical formations. Then, after 3 hours, changes were observed also in the reaction of the cerebral cortex to ether.

Experiments with the use of 8-10% carbon dioxide gas mixture had several qualitative differences (see the Figure). Thus under these conditions the first changes in the reaction of the central nervous system appeared from the side of the cortex (after one hour), and then the dynamics of the change in sensitivity to the narcotics was the same as in the experiments using 3 - 5% CO_2. The obtained facts can be explained by the fact that the specific retarding effect of the carbon dioxide on the central nervous system has different points of application as a function of its concentration in the inhaled gas mixture. Apparently the small concentrations (3 - 5%) first of all produce functional changes in the region of the subcortical formations, which appear as changes both in the humoral and in the nerve regulation of breathing and blood circulation [5,6,16]. The higher concentrations of carbon dioxide (8 - 10%) are characterized by the suppression of the effect on the cortical structures of the brain as a result of the appearance of its narcotic properties [3,6,10,14,17,18]. /209

TABLE 2. DURATION OF INTRANARCON NARCOSIS IN WHITE MICE IN BREATHING A HYPERCAPNIC GAS MIXTURE, MIN. (AVERAGE DATA).

Time of Residence in Gas Environment, hours	Statistical Index	CO_2 Content in Gas Mixture, %: 3—5 Cont.	3—5 Exp.	8—10 Cont.	8—10 Exp.
1	$M \pm m$	65,4±14,95	76,2±18,2	51,25±8,96	54,22±10,98
	% of control	—	116,3	—	105,7
	t	—	0,46	—	0,21
2	$M \pm m$	84,9±10,1	129,2±15,82	30,0±7,55	72,9±10,68
	% of control	—	152,3	—	243,0
	t	—	2,31	—	2,85
3	$M \pm m$	107±13,74	105±17,96	89±12,3	73,8±9,34
	% of control	—	98,2	—	83,1
	t	—	0,09	—	0,98
4	$M \pm m$	90,4±17,1	79,5±13,16	49,1±11,4	51,6±16,0
	% of control	—	88,0	—	105,0
	t	—	0,50	—	0,12

t = criteria of reliability of the difference in average values.

It should be shown that according to the data obtained, in the process of adaptation of the white mice to hypercapnia, approximately on the fourth hour a tendency was observed to normalization of the cortico-subcortical interrelationships in the central nervous system. Whether this serves as a sign of future adaptation to changed conditions of the gas environment or whether it reflects only the transitional period to the next phase change of the functional tonus of the various parts of the nervous system will necessitate special experiments.

Thus, in conclusion let us note that the methods of studying /210 the changes in the functional condition of the central nervous system by investigating the characteristics of the reaction to pharmacologicial compounds with different points of application permitted obtaining objective data on the different mechanism of the functional changes in the organism as a function of the concentration and duration of the effect of the carbon dioxide gas mixtures.

CONCLUSIONS

1. Prolonged residence in a hypercapnic gas environment is accompanied by phase changes in the reaction of the animals to narcotic remedies.

2. Change in the reaction to narcotics indicates a disruption in the functional interrelationships between the cortex and the subcortical structures of the brain.

3. Adaptation of animals to a hypercapnic gas environment with 3 - 5% carbon dioxide content is accompanied by the appearance of signs of retardation first of the subcortical formations.

4. A prolonged effect of the gas environment with 8 - 10% carbon dioxide is associated in first order with the cortical structures of the brain.

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ENZYMATIC ACTIVITY OF MONOAMINO-OXYDASE IN VARIOUS TISSUES AND ORGANS OF EXPERIMENTAL ANIMALS ACTED ON BY SEVERAL EXTREME FACTORS*

Report 1. Activity of Monoamino-Oxydase in Various Tissues and Organs of White Rats Under Ordinary Conditions and with Adaptation to Chronic Hypoxia.

Yu. N. Kopayev, Ye. F. Kotovskiy, V. V. Korolev, Yu. N. Korolev, and L. L. Shimkevich

ABSTRACT: In the experiments of white rats we studied the activity of monoamino-oxydase in tissues of the lungs, the kidneys, the liver, the pancreas and the skin. In the control animals the greatest activity of the monoamino-oxydase appears in the peripheral nerve, the cells of the vegetative nervous plexus and in the epithelium of the intestines and the parynchemal elements of the liver and the pancreas. With adaptation to chronic hypoxia we detected a significant lowering of activity of the monoamino-oxydase in the majority of tissues and organs. The activity of the monoamino-oxydase was quickly recovered. This phenomenon is one of the signs of adaptation to chronic hypoxia at the cellular level.

/211

* Article Not Translated.

ENZYMATIC ACTIVITY OF MONOAMINO-OXYDASE IN VARIOUS TISSUES AND ORGANS OF EXPERIMENTAL ANIMALS ACTED ON BY SEVERAL EXTREME FACTORS.*

Report 2. Activity of Monoamino-Oxydase in Different Tissues and Organs of White Rats Acted on by G-Loads.

Ye. F. Kotovskiy, V. V. Korolev, Yu. N. Korolev, L. L. Shimkevich and Yu. N. Kopayev

ABSTRACT: We studied the activity of monoamino-oxydase in the lungs, the kidneys, the liver, the pancreas and the small and large intestines using a histochemical method in the animals who were subjected to the effect of transverse G-loads (chest-spine) with a value of 25 units for a period of 10 minutes. In all the investigations of the organs we observed a slight decrease in the activity of the enzyme. The data obtained are studied from the point of view of mechanisms of cellular adaptation.

/218

* Article Not Translated.

ACTIVITY OF DEHYDROGENASES OF SUCCINIC AND LACTIC ACIDS UNDER CONDITIONS OF CHRONIC HYPOXIA.*

L. L. Shimkevich, Yu. N. Kopayev, Ye. F. Kotovskiy, V. V. Korolev and Yu. N. Korolev.

ABSTRACT: In experiments on white rats we made a histochemical investigation of the activity of dehydrogenases of succinic and lactic acids during acclimatization of animals under conditions of chronic hypoxia. We showed that under the given experimental conditions in the majority of organs a decrease occurs in the activity of the dehydrogenase of the succinic acid and an increase in the activity of the dehydrogenases of the lactic acid. We cite data on the characteristics of the adaptive changes in different tissues and organs. The results obtained are discussed from the viewpoint of the mechanisms of cellular adaptation, which is a part of the overall adaptation of the organism to oxygen deficiency.

/222

* Article Not Translated.

THE EFFECT OF HYPOXIA ON THE REACTION TO SEVERAL PHARMACOLOGICAL COMPOUNDS.

V. Ye. Belay, P. V. Vasil'yev, G. D. Glod and M. I. Bryuzgina.

ABSTRACT: In experiments on white mice we studied the influence of breathing a hypoxic gas mixture (7.5 - 9.0% O_2) for a period of 1 - 4 hours on the reaction to ether, intranarcon and corasole. We established that the effect of hypoxia is associated with phase changes in the sensitivity of the animals to pharmacological compounds; the narcotic effect of ether and intranarcon is increased and the sensitivity to toxic doses of corasole is decreased. We make the conclusion that change in the reaction to the compounds under the influence of hypoxia indicates functional changes in the central nervous system with preferential development of the process of inhibition.

The problem of oxygen starvation of the organism belongs among /230 the number of very real problems in the field of physiology. Numerous studies have shown that hypoxia is accompanied by distinct changes in the functional state of different systems of the organism; its reaction to several infectious agents and other pathogenic factors is changed [1,2,14,15]. N. M. Dmitriyeva [8,9] observed a change in the reaction of the organism to cardiac glucosides with experimental hypoxia. In this respect it is of undoubted theoretical and practical interest to investigate the characteristics of the pharmacodynamics of various medicinal compounds under conditions of oxygen starvation.

In the present paper we have studied the influence of hypoxia of different durations on the reaction to several narcotics (ether, intranarcon) and analeptics (corasole).

The experiments were carried out on 480 white male mice weighing 22 - 25 g. The animals were subjected for a period of 1 - 4 hours to the effect of a hypoxic gas mixture containing 7.5 - 9.0% oxygen (the carbon dioxide content did not exceed 1 - 1.5%) in a chamber with a volume of 50 liters. The composition of the gas atmosphere was controlled with an oxygen tester and a capnograph from the firm "Godart".

Five control and five experimental animals were simultaneously given an ether narcotic in a hermetically sealed exsiccator with a volume of 9.1 liters for a period of 15 minutes with a vapor concentration of 300 mg/liter. Intranarcon in a dose of 130 - 150 mg/kg

and corasole (80 - 90 mg/kg) were injected intraperitoneally in 0.1 ml solution per 10 g of animal weight.

The sign of the reaction to intranarcon was the total time of narcosis in stages III-IV following Schoen [18,19], and in the experiments with ether, the duration of the period of awakening after cessation of narcotization. We judged the reaction of corasole from the death rate of the animals. The experimental data were analyzed statistically [13].

Immediately after placing the animals into the hypoxia atmosphere we observed in them a distinct increase in frequency and deepening of respiration, the color of the eyes took on a bluish tint, clear signs of motive stimulation were noted. After 30 - 40 minutes the animals quieted down and then no further substantial differences were noted in their behavior as compared with the control animals. The dyspnea and bluish coloration of the eyes were retained for the entire period of residence in the chamber. Study of the sensitivity to pharmacological compounds for the different periods of time of the effect of the hypoxic gas mixture permitted distinct changes to be shown in the reaction of the animals. Generalized data on the influence of hypoxia on the reaction to intranarcon are shown on Table 1. /231

TABLE 1. INFLUENCE OF HYPOXIA ON THE DURATION OF INTRANARCON NARCOSIS IN WHITE MICE.

Time of Residence in Hypoxic Atmosphere, hours	Dose of Compound mg/km	Statistical Sign	Control	Experiment
1	150,0	$M \pm m$	113,6±14,3	150,3±14,42
		% of Control	—	132,3
2	130,0	$M \pm m$	24,8±4,42	35,4±6,34
		% of Control	—	143,0
3	130,0	$M \pm m$	30,8±8,15	42,6±8,37
		% of Control	—	138,5
4	150,0	$M \pm m$	76,6±9,84	79,2±14,6
		% of Control	—	103,0

From the data given in the table it is clear that after different periods of residence of the white mice in a hypoxic gas atmosphere we noted an increase in their sensitivity with respect to the intranarcon. The most pronounced changes in the reaction were observed after 1 hour of breathing the hypoxic gas mixture (t^1 = 1.8); in the later periods (after 2 and 3 hours) the differences between the experimental and the control groups gradually decreased (t = 1.37 - 1.0) and after 4 hours practically disappeared (t = 0.15).

Taking into account the data known from the literature on the dependence of the pharmacodynamic effect of the compound on the functional state of the organism, and especially on the functional state of the physiological system which is primarily affected by the medicinal compound [11] we may assume that under the influence of breathing a hypoxic gas mixture the functional cortico-subcortical interrelationships in the central nervous system are changed. /232 Here apparently at the beginning of adaptation of the mice to hypoxia the functional tonus of the subcortical formations is characterized by a slight prevalence of the inhibition processes.

TABLE 2. INFLUENCE OF HYPOXIA ON THE DURATION OF THE INVERSE DEVELOPMENT OF ETHER NARCOSIS IN WHITE MICE.

Time of Residence in Hypoxic Atomsphere, hours	Statistical Sign	Control	Experiment
1	$M \pm m$ %	3,4±0,32 —	6,12±0,35 180,0
2	$M \pm m$ %	4,58±0,67 —	4,53±0,60 99,0
3	$M \pm m$ %	5,25±0,51 —	5,0±0,55 95,2
4	$M \pm m$ %	4,85±0,42 —	5,29±0,4 109,0

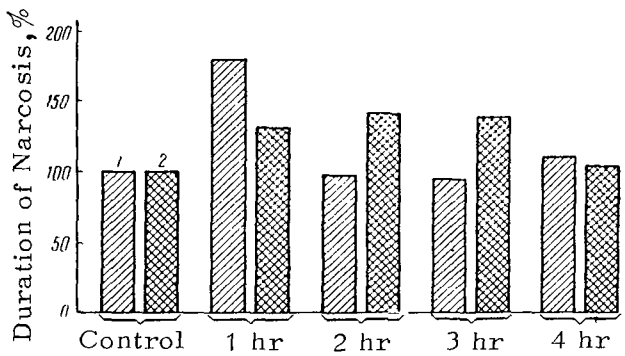
From the data given in Table 2 it is clear that breathing a hypoxic gas mixture produces in the white mice, after 1 hour, more

[1] The degree of reliability of differences between the control and the experimental animals.

pronounced changes in the sensitivity to ether than to intranarcon. In fact the duration of the inverse development of ether narcosis in these animals was substantially increased (t = 5.78). In subsequent times (2, 3 and 4 hours) no pronounced deviations were observed in the reaction to the compound being tested (see the figure).

If we assume that ether in average doses is a typical cortical narcotic [10], then we may assume that the process of inhibition at the beginning of the effect of the hypoxic mixture primarily involved the cortical structures of the brain. Along with this, the experimental results may also show a more rapid recovery of the cortical tonus of the major hemispheres. These assumptions fully agree with the literature data which indicate a greater vulnerability and a greater plasticity of the brain in comparison with the subcortical structures. Thus, the data on the reaction of the organism to narcotic compounds show that even from the first hour of adaptation to hypoxia in the cortex and the subcortical formations the processes of inhibition prevail. The increased motive activity of the animals during the first 30 - 40 minutes of breathing the hypoxic gas mixture indicates apparently the appearance of the first phase in the changes in the functional state of the central parts of the nervous system, i.e., the phase of stimulation.

/233



Influence of Hypoxia on the Duration of Ether (1) and Intranarcon (2) Narcosis.

TABLE 3. INFLUENCE OF HYPOXIA ON THE REACTION OF WHITE MICE TO CORASOLE.

Time of Residence in Hypoxic Atmosphere, hours	Dose of Compound mg/km	Control $P \pm m$	Experiment $P \pm m$
1	80.0—90.0	45±7.96	42±7.97
2	80.0—90.0	22.5±6.69	17.5±6.1
3	80.0—90.0	42.5±7.92	30.0±7.34
4	80.0—90.0	32.5±7.5	30.0±7.34

P ± m is the % of death rate with mean error. In each group of animals 20 of the mice received corasole in a dose of 80.0 mg/kg, and the other 20 animals received 90.0 mg/kg.

The data given on the changes in the functional state of the central nervous system under the influence of hypoxia was confirmed in the investigations with corasole (Table 3). In fact the death rate of the experimental animals in all the experiments was found /234 to be somewhat lower than in the control animals. Here the most pronounced differences were after 3 hours of breathing the hypoxic mixture (t = 1.16).

As we know, corasole exerts a stimulating effect primarily on the subcortical formations of the brain [4,5,11], being in large doses a convulsive poison. There are also indications that its effect is propagated diffusely both to the stem part of the brain and to its subcortical structures and to the cortical formations of the major hemispheres [16 - 18]. Therefore the decrease in the toxic effect of the compound in the experimental mice obviously is due to the development of inhibition processes in the central nervous system under the influence of oxygen starvation.

The effect of different pharmacological compounds, and especially narcotics, for the period of oxygen starvation has been studied by many authors [3,6,7,12], however necessary attention has not been given to the characteristics of the pharmacodynamics of the compounds being tested in the state of hypoxia.

The results of the experiments which we carried out indicate that the process of "acute acclimatization" to hypoxia is accompanied by pronounced deviations in the reaction of the organism to several pharmacological compounds.

CONCLUSIONS

1. Residence of white mice under hypoxic conditions (7.5 - 9.0% O_2) with a duration up to four hours is accompanied by phase changes in their reaction to ether, intranarcon and corasole.

2. Under the influence of hypoxia the narcotic effect of ether and intranarcon is increased, and the sensitivity to toxic doses of corasole is decreased.

3. Change under the influence of oxygen starvation in the reaction of the organism to pharmacological compounds indicates a development in the central nervous system of the process of inhibition.

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THE EFFECT OF ANTIOXIDANTS ON RESISTANCE OF THE ORGANISM AND CERTAIN FUNCTIONS UNDER HYPOXIA.

Ye. Ya. Kaplan and V. V. Ogleznev

ABSTRACT: In the present paper we studied the influence of antioxidants (ionole, propylgallate, BE-57, ambunole, mexamine) on the individual functions of the organism of animals (white mice, rats) and their tolerance to hypoxic hypoxia. We established that antioxidants increase the tolerance of the organism in rats and mice to acute, subacute and chronic hypoxia. An especially firm increase in tolerance to hypoxia was noted after repeated injection of mexamine. Here we observed smaller changes in the latent time of the motive reflex and more distinct changes in the stimulating process in the brain of the animals. After injection of the mexamine the oxygen requirement of the animals was lowered.

One of the means for increasing tolerance of the organism to /235
oxygen starvation is the use of pharmacological compounds.

Bearing in mind that the activization of oxidizing processes in the cells, by leading to an increase in oxygen requirement, lowers the tolerance to hypoxia (hyperthyreosis, fever, etc.), it is important to explain the effectiveness of the compounds which lower the tissue respiration, thus facilitating a better tolerance to oxygen starvation. As an example we can look at the increased tolerance of animals to oxygen starvation under conditions of hibernation, and also under certain narcotic states [1, 3, 7, 8].

It is natural to assume that during hypoxia it may be effective to use compounds from the group of antioxidants. However, there is as yet no unified opinion on this problem. Certain authors, by using indolilalkylamines and mercaptoalkylamines, observed a decrease in the tolerance to hypoxia; others, after preliminary doses of aminoethylisothiuronium- bromide-hydrobromide (AET), serotonin and other compounds from the group of indole derivatives on the contrary noted an increase in the tolerance of animals to hypoxia.

The purpose of this paper is to further study the problem of /236
the effect of antioxidants on the tolerance ot hypoxia and to investigate individual functions of the organism.

We used the following antioxidants: ionole (300 mg/kg), propylgallate (40 mg/kg), BE-57 (300 mg/kg), ambunole (40 mg/kg), synthesized in the laboratory of N. M. Emanuel and mexamine (5-methoxy-

triptamine, 200 mg/kg), produced by Prof. N. N. Suvorov. For comparison we also investigated several natural compounds of plant and animal origin, i.e., eleutherococcus, muscile adenylic preparation (MAP), vitamins B complex. The first four preparations were injected subcutaneously, the others were given per os.

Four series of investigations were carried out on 514 white mice of both sexes weighing 18 - 25 g.

In the first series we studied the tolerance of the animals to acute oxygen starvation in 289 mice after a single injection of the preparations under study.

In the second series we investigated the effect of multiple injection of the preparations in 95 mice on the tolerance of the animals to acute hypoxia.

In the third series we found the latent time of the motive reflex and the ability to summation of the subthreshold impulses following V.V. Zakusov on 70 mice adapted to hypoxia.

In the fourth series in 60 animals before and after the effect of oxygen starvation we determined the sorption capacity of the proteins of the brain tissue by the method of vital stain (following D.N. Nasonov). As the standard of adaptation to hypoxia we used animals, who had undergone acclimatization to high altitudes (16 days, 2000 m and 14 days, 3700 m). The animals were subjected to the effect of acute hypoxia by "ascent" to an altitude of 9000 m in an exsiccator at a rate of 3 km/minute. The animals were kept at this altitude for 5 minutes, after which they were raised still another kilometer and kept there for the next five minutes. Further ascents after five-minute intervals continued until breathing ceased in the animal.

Data on the effect of a single injection of the preparations under analysis on the survival of animals under conditions of acute hypoxia are shown on Figure 1. As is obvious from the figure, the preparations from the group of antioxidants have a more pronounced effect in comparison with the other materials and substantially increase the tolerance of the animals to oxygen starvation.

In the next series of experiments we studied the effect of multiple injection of mexamine into the organism. As is obvious from the diagram in Figure 2, the tolerance of the animals to hypoxia is increased in proportion to the increase in the time of the effect of the preparation. The animals reach a tolerance that is similar to that observed in them after prolonged residence at high altitude. An especially firm increase in tolerance to hypoxia was observed in /237
the animals after multiple injection of mexamine. This is clear from Figure 3, on which the results are shown from studying the tolerance to acute hypoxia of animals after a lapse of three days following cessation of the dose of preparations of mexamine,

cystophose and petroleum growing substances (PGS); the animals received the preparations daily for a period of 6 days.

The use of antioxidants also facilitates a better tolerance of prolonged acting (for a period of 30 days) hypoxia.

Since many adaptation reactions which occur in the organism involved participation of the central nervous system, it is important

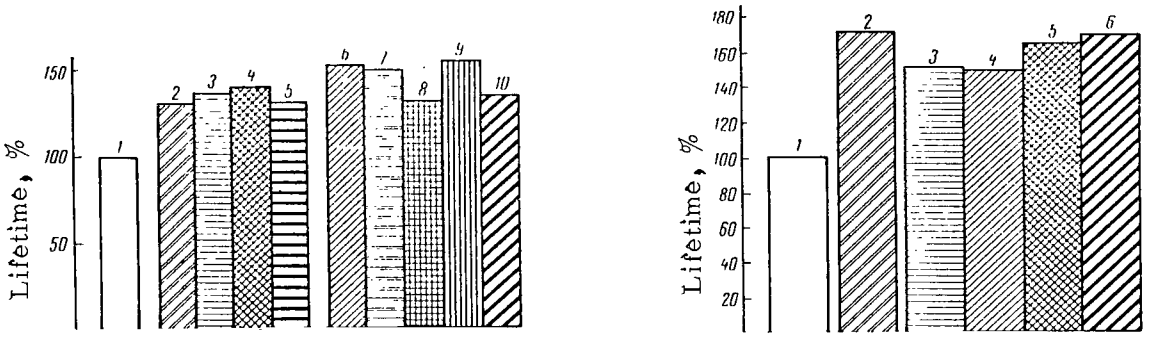

Fig. 1: Survival of Mice Under Conditions of Acute Hypoxia After Single Dose of Pharmacoligical Preparations. 1. Control. Stimulants and Tone-Up Preparations; 2. Eleuthrococcus; 3. Hormone Preparation; 4. MAP; 5. Mixture of Vitamins B Complex. Antioxidants; 6. Mexamine; 7. Ambunol; 8. Ionole; 9. BE-57; 10. Propylgallate.

Fig. 2: Survival of Mice Under Conditions of Acute Hypoxia with Multiple Doses of Mexamine. 1. Control; 2. Conditioned at High Altitude; 3. Single Dose of Mexamine; 4. 6 Doses; 5. 10 Doses; 6. 15 Doses.

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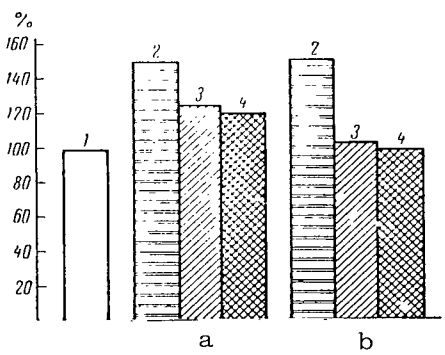

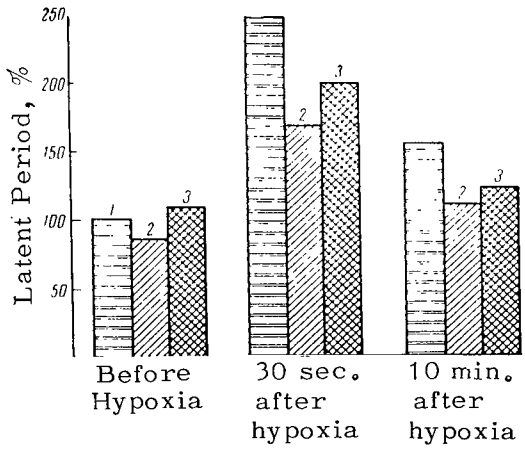

Fig. 3: Change in the Tolerance of Mice to Hypoxia After Cessation of the Dose of Preparations. a. Immediately After Taking the Preparation for Six Days; b. After Three Days. 1. Control; 2. Mexamine; 3. Cystophose; 4. PGS.

Fig. 4: Effect of Mexamine on the Latent Period of Motive Reaction in Mice Under Acute Hypoxia. 1. Control; 2. Conditioned at High Altitude; 3. After Taking Mexamine.

to investigate several characteristics of its functional state.

We found that a prophylactic dose of mexamine facilitates a smaller change in the latent time of the motive reflex after hypoxic adaptation. This effect, in its character, was found to be near the effect observed in animals acclimatized at high altitude (the investigations of V.V. Malkin, et al.). He noted this both immediately after the effect to hypoxia and later, after 10 minutes (Fig. 4).

The obtained data indicate a positive effect from mexamine on the function of the central nervous system under hypoxia. /239

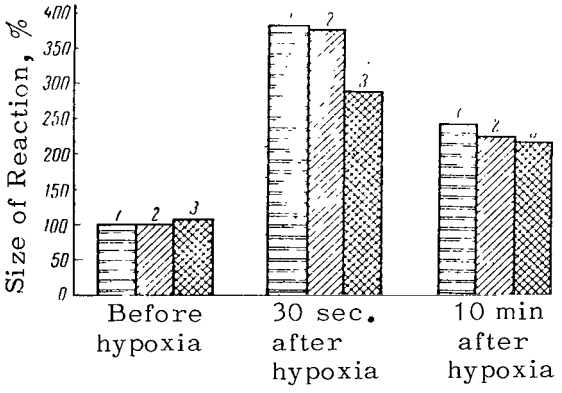

Fig. 5. Effect of Mexamine on the Summation of Subthreshold Impulses in Mice Under Acute Hypoxia. The Designations are the Same as in Figure 4.

In this paper we have studied the capacity of mice for summation of subthreshold impulses. The essence of this phenomenon, found by I. M. Sechenov, at the present time is widely known. The results of the experiments are shown on Figure 5. As is obvious from the diagrams, in the experimental mice, to obtain a summation effect following the effect of hypoxia a smaller number of subthreshold impulses is required than in the control animals. A similar result was found also in the investigations carried out on animals acclimatized at high altitude.

Since the capacity for summation of subthreshold impulses is associated with the degree of excitability of the nerve cells, these data indicate fewer disruptions in the exciting process in the brain of animals who have received the preparation.

In the next series of experiments, using the method of vital staining of the tissues we studied the degree of alteration of the brain cells under hypoxia after taking mexamine. As is obvious from these data (Fig. 6), in the animals who have received mexamine and who were acclimatized at high altitude, following the effect of hypoxia there was a smaller sorption of the stain than in the control animals. This indicates a lesser alteration of the brain tissue.

Thus, the obtained experimental data indicate that the use of preparations from the group of antioxidants is promising in the struggle against oxygen starvation. Along with this we still do not know enough about the mechanism of the effect of the individual antioxidants, thus making it difficult to understand their defense /240

role during hypoxia. An explanation of the mechanism of the effect of preparations from this group will permit a more rational use of them for the purpose of influencing the character of the metabolic processes in the organism.

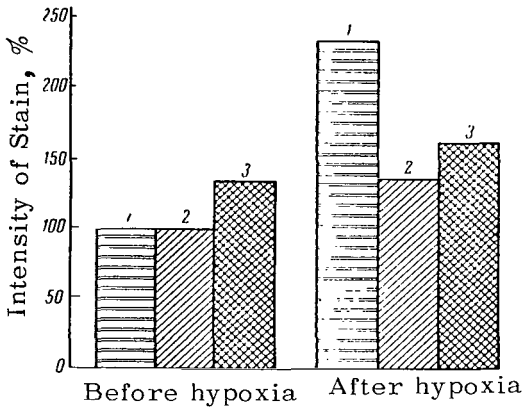

Fig. 6. Effect of Mexamine on the Staining of the Brain of Mice under Acute Hypoxia. The Designations are the Same as in Figure 4.

At the second stage of the investigation we studied in the animals the intensity of the oxidizing processes in the tissues before and after injection of mexamine.

The investigations were carried out on 58 white rats and 40 white mice. The mexamine was injected subcutaneously, 15 mg per 1 kg of weight. We judged the intensity of the oxidizing processes in the tissues from the amount of oxygen required. This latter was determined by Kalabukhov's method.

In the first series of experiments the investigations were carried out under conditions of subacute hypoxia. The animals were placed into exsiccators where they breathed a gas mixture for four hours that contained 7.5% oxygen, which corresponds to a partial pressure of this gas at an altitude of 8000 m.

Analysis of the material obtained showed that mexamine, both under normal conditions and under hypoxia, lowers the oxygen requirement in rats and mice. The oxygen requirement of the animals, 40 minutes following injection of mexamine, was lowered on the average to 36 cm^3/hr (per 100 g of animal weight). Under hypoxic conditions, we observed in the animals a further decrease in the oxygen requirement. After 4 hours of breathing the hypoxic mixture of oxygen requirement was lowered still to 53 cm^3. The oxygen requirement in the control animals was also lowered to approximately the same value. The results obtained confirm the data of Ye.M. Kreps, N.A. Verzhbinskaya, Ye.Yu. Chenykayeva, Ye.V. Charkovskaya and Ts.K. Gavurina [4] as to the decrease in oxygen requirement under hypoxic conditions in unadapted animals. /241

A decrease in oxygen requirement in the experimental rats in comparison with the control animals was noted also by us in the experiment with chronic hypoxia.

Thus, the results of the investigations indicate the capacity of the mexamine to lower the intensity of the oxidizing processes in the tissues. Obviously, mexamine, by playing the role of an

inhibitor, facilitates a more economic consumption of oxygen entering the organism.

Processes of oxidation occur in the tissues of two types (free and associated with phosphorylation). It is important to explain the effect of mexamine on each of these types with respect to solving the problem of the mechanism of the effect of antioxidants on tissue respiration. We made special investigations where, as the inhibitor, we used sodium amytal. We know that this latter inhibits oxidation associated with phosphorylation, and free oxidation of hydrolytic type occurs inside the mitochondria of the cells [6]. We might assume that if the mexamine to any degree blocks the intramitochondrial free oxidation and the oxidation associated with phosphorylation, then the animals who have received this preparation can be assumed to be fully or partially amytal-resistant, i.e., they do not react to the injection of sodium amytal with a lowered oxygen requirement.

Based on this, in part of the experiments we injected the animals with sodium amytal subcutaneously with 6 mg per 100 g of weight 50 minutes following the injection of mexamine. The oxygen requirement in the animals was determined before and 40 minutes after injection of sodium amytal. The control group of animals was not injected with mexamine.

From analysis of the obtained material it was clear that on a background of the effect of mexamine, sodium amytal lowered the oxygen requirement to a lesser degree (Fig. 7). Such a result was observed both in carrying out the investigations under normal conditions and in a large part of the cases in the experiment with chronic hypoxia.

This fact permits the assumption that, in character of the effect on oxidizing processes in the cells, mexamine is similar to the effect of sodium amytal, which indicates the development of a stage of resistance (after Sel'ye). We can also come to this conclusion based on the current concepts that amytal-sensitive respiration is characteristic of the "anxiety" phase and amytal-resistant respiration is characteristic of the "resistance" phase of the total adaptation syndrome [6]. This confirms the data of V.G. Petrukhina (see this collection, p. 241, original text, p. 196, English text), who found a lower degree of histochemical and morphological changes in the adrenal cortex under hypoxia for rats after repeated injections of mexamine. /242

In conclusion we must note that in our investigations mexamine did not produce any pronounced decrease in the overall functional activity of the animals. This should be taken into account in interpreting questions of using antioxidants in practice.

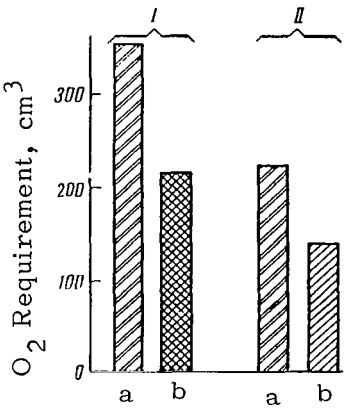

Fig. 7. Oxygen Requirement of Mice (cm per 100 g of Weight) Before and After Injection of Sodium Amytal (Average Data). I. Control Animals; II. On a Background of the Effect of Mexamine; a. Before Injection of Sodium Amytal; b. After Injection of Sodium Amytal.

CONCLUSIONS

1. Antioxidants increase the resistance of the organism in rats and mice to acute, subacute and chronic hypoxia.

2. After multiple injections of mexamine into rats, just as with acclimatization at high altitude, an increased tolerance arises to hypoxia.

3. The oxygen requirement under the influence of mexamine is lowered both under normal conditions and with oxygen deficiency.

4. The restructuring of the cell respiration, which occurs under the influence of mexamine and which is characterized by the decrease in oxygen required by the tissues, facilitates a better tolerance of the organism both to acute and to chronic hypoxia.

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THE PROBLEM OF THE MECHANISM OF THE EFFECT OF MEXAMINE UNDER HYPOXIA*

Ye.Ya. Kaplan, V.G. Petrukhin and V.I. Solov'yev

ABSTRACT: We studied the biochemical characteristics of the blood and the histochemical changes in the organs of mice subjected to the effect of acute, subacute and chronic hypoxia and the preliminary injection of mexamine. We found that single and repeated injections of mexamine were accompanied by a decrease in the pH, standard bicarbonate and the total amount of CO_2 in the blood, and by a slight suppression of the activity of the alkaline phosphatase, DPN-diaphorase and succinate-dehydrogenase in the liver, adrenal glands and the myocardium. Preliminary injection (once) before the effect of acute and subacute hypoxia, and also periodic injections before chronic hypoxia, lowered the degree of changes in the activity of the oxidizing ferments as well as the biochemical characteristics of the blood in comparision with that which was observed under the influence of a single hypoxia. The injection of mexamine facilitated a more rapid recovery of the structure in the organs. The defensive effect is manifested in the lowering of the oxidizing-recovery processes in the tissues under the influence of mexamine injections.

/243

* Article Not Translated.

THE EFFECT OF ATHLETIC TRAINING AND ACCLIMATIZATION UNDER MIDDLE-ALTITUDE CONDITIONS IN THE CAUCASUS ON SEVERAL CHARACTERISTICS OF THE PERIPHERAL BLOOD OF YOUNG FIELD AND TRACK ATHLETES

Ye. B. Gippenreyter

ABSTRACT: In youths and girls who have participated in field and track athletics, moving to mountainous areas produces changes in the blood: growth in the number of erythrocytes, reticulocytes and the amount of hemoglobin. In the athletes we found a decrease in the number of eosinophils in the blood which indicates activation of the function of the pituitary-adrenal system. In studying the process of acclimatization and conditioning of athletes it follows to take into account the reaction of the blood to hypoxia.

At the present time it has been strictly established that /254
changes in the peripheral blood are subtle signs of a reaction of the organism including conditions of oxygen deficiency. At the international symposium "Athletics at Middle Altitudes" held in December 1965 in Magglingen (Switzerland), it was noted that modern methods of investigation permit finding hematological changes even with a very insignificant decrease in the partial oxygen pressure in the atmospheric air even at an altitude of 800 - 1000 m above sea level.

We investigated the character and features of the changes in the peripheral blood of young field and track athletes in the process of a 33-day acclimatization and training under conditions of the Middle Caucasus (Terskol, altitude of 2000 m above sea level). By selecting as the object of the investigations a group of athletes during puberty, we proceeded from the fact that this age is of known interest since it is characterized by an increased sensitivity and lowered tolerance to hypoxia and less effective adaptation to it than in adults [7,8]. We took into account also the fact of studying the growth characteristics of the reaction of the organism of the athletes during the period of sexual maturation in connection with the observed tendency of "rejuvenascence" of the category of athletes of higher qualification in several types of sports, where record holders and champions of the continent, the world and the Olympic games are formed at this age.

The basic problem of this paper was an evaluation of the characteristic features and the dynamics of the changes in the peripheral blood as one of the signs of acclimatization to

conditions of middle altitude so that the obtained data could be used in developing recommendations for a training schedule for the athletes under mountainous conditions. Instructional observations were carried out by Trainer M. M. Bogen. They were combined with the best available investigations under mountainous conditions of several signs of internal breathing, the cardiovascular system, coordination of movements, etc.

METHOD

Study of the picture of the peripheral blood was carried out /255 by the methods ordinarily used.

We studied 10 field and track athletes (6 boys and 4 girls) of the third athletic rank who studied in the Children's Sports School of the Oktyabr'skiy District of Moscow, average age 16 years, athletic experience less than 1 year (8 months), specialization, sprinting, running middle distances and athletic walking. There was also a control group of boys and girls of the same age who actively participated in sports at high altitude.

The blood was taken before leaving Moscow, on the 3rd, 9th, 18th, 20th and 30th day of residence in the region near Mt. Elbrus, and on the 6th and 20th day of deacclimatization; in the control group on the 2nd, 11th and 20th day of residence at high altitude.

We studied the dynamics of the change in the number of erythrocutes, reticulocytes, the hemoglobin, the eosinophils, the hemocrit number, the oxygen capacity of the blood, the color index and the amount of hemoglobin in each erythrocyte (these latter three indices were computed by formulas).

RESULTS

In the obtained data we are concerned with the quite moderate changes in the red blood characteristics. Thus, in the boy athletes the number of erythrocytes, after one month training and acclimatization at high altitude, increased on an average by 330,000 (6.7%), reaching 5,230,000 which exceeds the physiological norm only slightly (Fig. 1). The concentration of hemoglobin on the 20th - 30th days of residence in the mountains increased on the average by 10% (from 14.8 to 16.2%), reaching the upper boundary of the normal. Reticulocytosis was also moderate (Fig. 2). The original amount of hemoglobin in one erythrocyte was 30 μμg, on the 20th day it increased to 33.0 μμg, i.e., by 7.5%. The oxygen capacity of the blood also increased by the end of the 3rd - 4th week at high altitude by 9 - 10%, reaching 21.7 - 21.8 volume percent. The color index did not exceed the normal range.

In the control group the increase in the red blood characteristics also had a moderate character, but in correlation with the second day at high altitude the subsequent changes were stronger

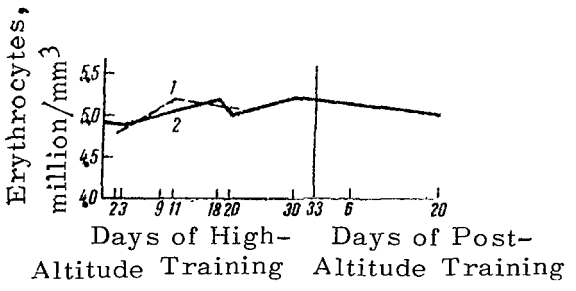

Fig. 1. Change in the Number of Erythrocytes During Adaptation at High Altitude and After Descent in the Control (1) and the Experimental (2) Groups.

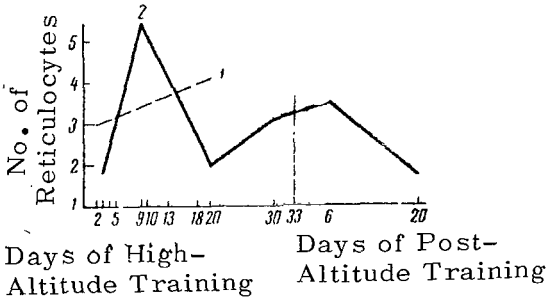

Fig. 2. Change in the Number of Reticulocytes During High-Altitude Adaptation. Here and in Figures 3 - 6, the Designations are the Same as in Figure 1.

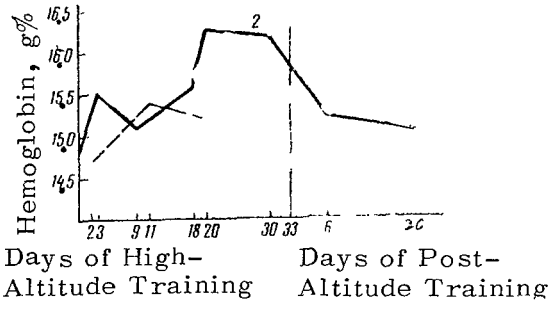

Fig. 3. Change in the Amount of Hemoglobin During High-Altitude Adaptation.

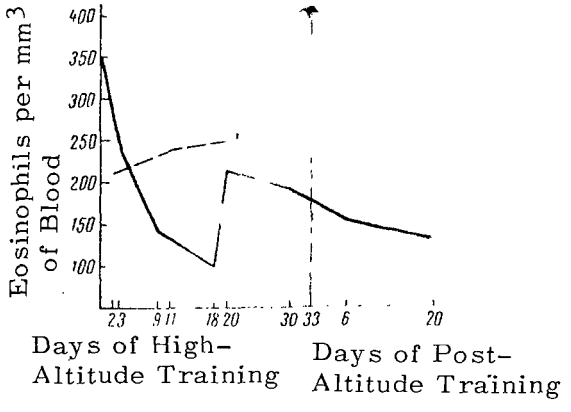

Fig. 4. Change in the Number of Eosinophils During High-Altitude Adaptation.

than in the field and track athletes. Thus the number of erythrocytes on the 11th and 20th days of residence in Terskol in the control group exceeded the value of the first days by 7 - 8%, and in the sports group the relative increase in comparison with the second day was on the average 2%. The number of reticulocytes on the 20th day increased in the control group from 10,045 to 20,913, i.e., it doubled, and in the field track athletes from 8745 to 10,163, i.e., by only 16%. The absolute values of the amount of hemoglobin, the color index, the oxygen capacity of the blood and /257
the amount of hemoglobin in one erythrocyte in the control group were lower in the mountains than in the experimental group (Fig. 3).

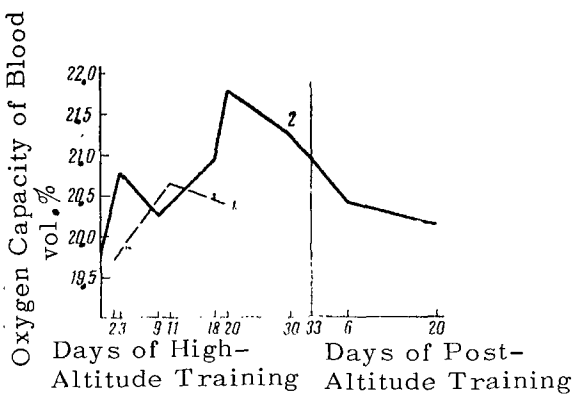

Fig. 5. Change in the Oxygen Capacity of the Blood During High-Altitude Adaptation.

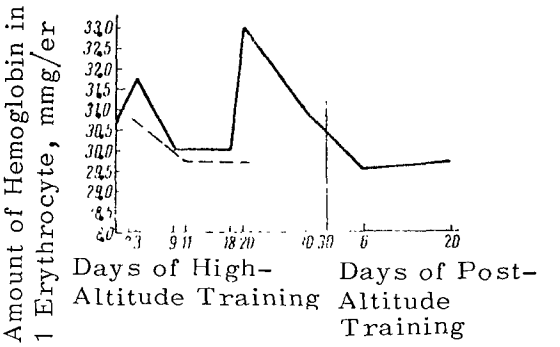

Fig. 6. Change in the Amount of Hemoglobin in One Erythrocyte During High-Altitude Adaptation.

The eosinophil leukocytes showed a significant and firm decrease in the athletes. In the first days the number decreased on an average by 32%, by the 9th day by 60%, by the 18th day it dropped by 72% and by the end of residence at high altitude it remained lower than the original value by 45%. In the control group, no eosinopenia was noted. (Fig. 4).

On the background on an overall picture of insignificant changes we observed substantial individual differences in the degree and character of the reaction of the subjects' blood. In several of the field and track athletes with low original data, the hematological changes were rather significant both in absolute and in relative values (13.3 g% and 4,500,000 erythrocytes per mm^3 of blood); by the 30th day at high altitude they increased respectively to 17 g% and 5,820,000, i.e., by 29.3%; in O. M-va, from 12.9% and 4,200,000 respectively to 15.9% and 5,200,000, i.e., by 23% of the original level (Fig. 5).

Along with this in the subjects with a high initial amount of /258
hemoglobin and number of erythrocytes, the relative changes were very weakly expressed. Thus, in B. M-n the number of red blood corpuscles by the end of residence at high altitude increased from

5,650,000 to 5,940,000, i.e., by 290,000 or 5%, and the concentration of hemoglobin after a series of fluctuations returned to the same level as before the expedition into the mountains, i.e., 17.8 g%.

Individual characteristics in the reaction of the blood appeared also in that at the beginning of residence at high altitude we observed in several of the subjects a simultaneous decrease in the number of erythrocytes and the hemoglobin (B. M-n), in others, a drop in the erythrocytes and an increase in hemoglobin (N. N-ko); in still others we observed a simultaneous increase in these characteristics from the very first days of the high-altitude expedition (O. M-va). In several of the subjects the increase in the amount of hemoglobin was more pronounced than the increase in the number of erythrocytes (T. V-va), in others, on the contrary, the number of erythrocytes increased more strongly and the hemoglobin to a lesser degree (I. U-k, control group). In several of the subjects these two characteristics increased in parallel and to an equal degree, e.g., Kh. T-va (Fig. 6).

DISCUSSION

The data which we obtained indicate that among the changes in the physiological systems, the organism of the blood is one of the first to react to lowering the partial oxygen pressure in the inhaled air. The reaction is of an adaptive nature since it increases the supply of oxygen to the tissues.

The moderate degree of hematological changes in the boy athletes is obviously associated with the muscular load. As we know athletes possess an elevated tolerance to oxygen deficiency [12, 16, 18]. The significance of muscular activity as a nonspecific factor which increases the tolerance to hypoxia was seen in the experimental conditioning of animals as well [5].

Investigations carried out over a period of many years on athletes of different age, experience, qualification and specialization confirm the positive effect of being involved with prolonged and continuous exercises on adaptability (field and track, swimming) and on a better tolerance of the organism to motive hypoxemia and to altitude hypoxia [3, 4, 10].

However, we did not find that the young field and track athlethes differed in their good tolerance to altitude hypoxia. In the first days in the mountains even a small physical load was endured with difficulty: three-minute running at a slow pace led to dyspnea, compelling them to change to a walk (during the time of the load on the 1st day), an ascent of 200 m up the slope of the mountain produced vertigo in two of them (on the 3rd day) and nose bleed in one of them. Therefore, active conditioning was begun only from 6th day. The time required for athletic conditioning was rather long. Only from the 16th day were all the athletes /259

adapted well to loads, thus allowing their instructor to institute a new training schedule (data from M. M. Bogen).

It seems to us that the insufficiently high tolerance of the youthful athletes to hypoxia at high altitude is apparently explained by their growth characteristics in this respect, and also by their comparatively brief experience in sports. Furthermore, it follows to take into account that one hypoxic conditioning for being involved with continuous exercises under low-altitude or pressure-chamber conditions is insufficient for raising the altitude tolerance, since not only the hypoxic factor exerts an influence on the process of adaptation of the organism to middle altitudes, but many other specific factors of the mountainous climate as well: temperature and dryness of the air, intensity of solar radiation, etc.

In light of the data from the trainers' observations on the overall state of being and the dynamics of the athletic functional capacity we may assume that the lack of clearly expressed changes in the red blood system of the athletes is probably explained by the extremely high physiological load which could inhibit stimulation of hemopoiesis.

The changes in the blood characteristics which we observed were of a phase character which was apparently due to the effect of the hypoxic factor (motive hypoxemia in conjunction with hypoxic hypoxia) and the regularities of the hemopoiesis.

It is interesting that in five of the young athletes during the first two-three days of residence at high altitude we observed a brief drop in the number of erythrocytes. We may assume that this was due to the increased hemolysis of the erythrocytes. The drop in the number of erythrocytes was noted some time ago by several investigators [17, 20, 23]. N. N. Sirotinin et al repeatedly detected a drop in the erythrocytes and hemoglobin on the 2nd-3rd day of residence at high altitude [11]. Similar phenomena were observed by Ya. G. Uzhanskiy and others [14]. Gross and Kestner [19] found that in several cases the amount of hemoglobin in the blood was lowered in carrying out intensive muscular labor at high altitude. Reynafarje [22] assumes the reason for erythrodiuresis to be not only the suppression of the erythropoietic activity and the increased disruption of the erythrocytes, but the accelerated drop in red blood corpuscles at the site of formation in the brain even before entering the blood circulation.

In the other five athletes immediately upon entering the mountains an increase was noted in the red blood characteristics, the changes in the amount of hemoglobin being more pronounced than the increase in the number of erythrocytes. During the first days the increase in the number of red blood corpuscles occurred because of the reflex mobilization of the erythrocytes from the blood depot /260 and in subsequent days as a result of actual hemopoiesis.

For reasons which are unclear to us the number of eosinophils in the youthful athletes prior to the mountain trip was at a high level, 354 with 50 - 200 per mm^3 of blood being normal. After being decreased to a pronounced and firm degree in Terskol, it no longer exceeded the normal ranges.

The eosinopenial reaction of the peripheral blood of humans during ascent to high altitude was noted by M. Khalkhuber and F. Gabl and by J. Milledge and H. Tatsunuma and by the Russian scientists P. V. Beloshitskiy et al [2, 20, 21, 24]. The drop in the number of eosinophils reflects apparently the development of the reaction of "stress" and is caused by changes in the functional state of the pituitary and the adrenal cortex. The stress effect of the intense muscular load under conditions of altitude hypoxia activized the activity of the pituitary-adrenal system which in turn suppressed the activity of the formation of eosinophils. In the control group because of the lack of any large physical load there were no stress-reactions and therefore the number of eosinophils did not decrease.

CONCLUSIONS

1. Moving to a mountainous locality produces regular adaptation reactions in the red blood. They are of a phase character and have wide individual fluctuations.

Redistributional and actual hemopoiesis and erythropoiesis increase the respiratory surface of the blood and thus improves the supply of oxygen to the organism under hypoxic conditions.

2. We may assume that the lack of strongly expressed hematological changes in the young athletes can be explained not only by the moderate altitude and the relatively short period of residence in the mountains, but is also associated with the muscular load.

3. The drop and the firm retention of the number of eosinophils in the peripheral blood of the athletes at a decreased level and the lack of this decrease in the control group indicates activation of the function of the pituitary-adrenal system as a stress-reaction to the intense muscular activity under conditions of oxygen deficiency.

4. In studying the process of acclimatization and conditioning of athletes under middle-altitude conditions it follows to take into account the individual characteristics of the reaction of the blood to hypoxia.

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/261

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Translated for the National Aeronautics and Space Administration by:
Aztec School of Languages, Inc.,
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